SCIENCE

Vol. 109 No. 2832 Friday, April 8, 1949

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Science, a weekly journal founded in 1880, is published each Friday by the American Association for the Advancement of Science at the Business Press, 10 McGovern Ave., Lancaster, Pa. Editorial and Advertising Offices, 1515 Massachusetts Ave., N.W., Washington 5, D. C. Telephone, Executive 6060. Cable address, SCIMAG, Washington, D. C. Entered as second-class matter at the Post Office at Lancaster, Pa., January 13, 1948, under the Act of March 3, 1879. Acceptance for mailing at the special rate postage provided for in the Act of February 28, 1925, embodied in Paragraph 4, Sec. 538, P.L. and R., authorized January 13, 1948.

Manuscripts submitted for publication should be sent to the Editorial Office, with stamped, self-addressed envelope enclosed for possible return. The AAAS assumes no responsibility for the safety of the manuscripts or for the opinions expressed by contributors.

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The Neutron Pile as a Tool in Quantitative Analysis; The Gallium and Palladium Content of Iron Meteorites

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THE SCIENCE OF METEORITICS has come to be looked upon in recent years as a science of increasing importance, largely because of its recognized bearing upon astrophysical problems. In particular, it now appears likely that an intensive study of the distribution of elements in meteorites will enable one to draw important conclusions concerning the structure of planets, the origin of our solar system, and the relative "cosmic" abundances of the chemical elements (*1, 2*).

Unfortunately, with the exception of a very few common elements such as oxygen, silicon, magnesium, iron, nickel, and calcium, elements are found in meteorites in quantities of only a few parts per million (*3, 4*). Assaying the concentration of these rarer constituents of meteorites with an accuracy of 10% or better, as we often wish to do, presents grave analytical problems. V. M. Goldschmidt (*4*), Hevesy (*5*), and the Noddacks (*11*), who did much of the excellent earlier work on assaying the rarer constituents of meteorites, used at one time or another straightforward quantitative chemical methods, X-ray spectroscopy, and chemical spectroscopy. While their work has been very useful, the difficulties inherent in such analytical work gave rise to errors which appear in many cases to be greater than factors of two, and in some cases as great as a factor of ten.

If marked progress is to be made in the application of meteorites to cosmological problems, it seems clear that analytical techniques are needed which will satisfy the following criteria: (1) The method must permit an accuracy of 10% or better in determining the concentration of a given element present in the concentration range of 0.01 ppm to 500 ppm; (2) there must be no interferences from other chemical elements; (3) there must be no danger of contamination during the analysis; (4) the method must be reasonably rapid. A survey of various possible analytical approaches to the problem led the authors to the conclusion that a radiochemical technique offered the most promise.

The General Method. The concept of utilizing neutron activation as an analytical tool is by no means new. As early as 1936 Hevesy and Levi (*7*) applied the neutron activation method of analysis to the rare earth elements. They were able to find the 2½-hr dysprosium period in a sample of yttrium, after activation with neutrons, and thus demonstrated the presence of dysprosium impurity to an extent of 1%. Using the same method, Hevesy and Levi were also able to detect small amounts of europium in gadolinium samples (*8*). Since that time, modifications of the method have been used for semiquantitative studies of elements possessing relatively high neutron activation cross sections.

Most elements when irradiated by slow neutrons give rise to radioactive species of the same atomic number. The specific activity produced in a given element by neutron irradiation depends upon the neutron capture cross section of the isotope giving rise to the activity when it captures a neutron, the abundance of the isotope, the neutron flux, the half-life of the radioactive species, and the length of the irradiation: $a = N\sigma f(1 - e^{-\lambda t})$ where a = activity (disintegrations/sec), N = number of atoms of the nuclear species giving rise to the activity, σ = neutron capture cross section of species per atom (cm^2), f = neutron flux (neutrons/cm^2/sec), λ = decay constant of radioactive product, t = length of irradiation.

With the advent of the neutron pile, neutron fluxes capable of producing very high specific activities have become available. For example, the flux of the order of 10^{12} neutrons/cm^2/sec available in the heavy water pile at the Argonne National Laboratory is capable

[1] The authors wish to thank Professor Lincoln La Paz, of the Institute of Meteoritics, University of New Mexico, for many of the samples used in this study. We are also indebted to Dr. S. Roy, of the Chicago Natural History Museum, who supplied us with several specimens, to Mr. H. H. Nininger, of the American Meteorite Museum, who made available a number of specimens, and to Professor Cyril Smith, of the University of Chicago, who supplied us with a specimen of the Carleton meteorite. Mr. Richard Desvamps helped with much of the counting and with certain phases of the experimental work.

of producing, in many elements, specific activities of the order of magnitude of 100,000–1,000,000 disintegrations/min/μg of element. Such specific activities make it possible to carry out the following general procedure: (1) A portion of the substance to be analyzed is irradiated in the pile, together with a standard consisting of a known weight of the element being determined; (2) the unknown is dissolved and a known weight of the element being determined is added to the solution; (3) the element added is chemically processed in order to free it from the activities associated with other elements present in the unknown; (4) the chemical yield of the procedure is determined; (5) the activity of the element in the unknown is compared with that of the standard; and (6) the purity of each activity is checked by measurements of half-lives and absorption spectra.

TABLE 1

SENSITIVITY OF PILE ANALYTICAL METHOD FOR CERTAIN ELEMENTS
(Argonne Heavy Water Pile, 7-hr bombardment at highest flux)

Element	Sensitivity (μg)	Element	Sensitivity (μg)
Na	0.01	Cu	0.004
Si	0.3	Ga	0.01
P	0.4	Ge	2.0
S	700.0	As	0.005
K	0.1	Rb	1.0
Ca	100.0	Sr	300.0
Sc	0.3	Y	0.05
Ti	400.0	Zr	2.0
Cr	1.0	Mo	0.7
Mn	0.003	Pd	0.005
Fe	700.0	Ag	5.0
Ni	0.1	Dy	0.00001

Table 1 gives examples of the estimated sensitivity of the neutron irradiation method for various elements in the Argonne heavy water pile. The term "sensitivity" is used here in a sense differing somewhat from its usual connotation in connection with analytical methods. In this paper the term is used to indicate the smallest quantity of an element that will give rise to an activity sufficiently intense to permit the measurement of half-life and absorption after the element has been exposed to the central pile flux for a period of 7 hr. Thus "sensitivity" here denotes the smallest quantity of an element that can be measured with a precision better than 10%, utilizing the central flux of the Argonne Pile for a time not unduly long.

It can be seen that the sensitivities obtainable are in general quite satisfactory, and in some cases are remarkable. The cases of manganese, copper, arsenic, palladium, and dysprosium, shown in Table 1, are particularly noteworthy. If one assumes that a half-life of 30 min represents the shortest life-time practicable for analytical determination, then the method is applicable to about 60 of the 75 stable elements existing in nature (excluding the rare gases). The method either cannot be applied or can be applied only with difficulty to hydrogen, lithium, beryllium, boron, carbon, nitrogen, oxygen, fluorine, magnesium, aluminum, vanadium, cobalt, columbium, and rhodium. In general, the pile method of analysis is more sensitive for elements of odd atomic number than for elements of even atomic number, because nuclear species of odd mass number have larger activation cross sections and nuclear species giving rise to the activities in the even elements have generally low abundance.

Thus far the pile analysis method has been developed and tested for the elements gallium and palladium. The method has been applied extensively to the problem of analyzing iron meteorites for these elements. Gallium is present in iron meteorites to an extent of 10 to 100 ppm; palladium is present to an extent of 1 to 5 ppm.

The Method Applied to Gallium. Gallium is present in sufficient quantity in meteorites, and the activation cross section is sufficiently large, to permit the use of the more modest neutron fluxes obtainable some distance from the center of the Argonne pile.

Gallium has two stable isotopes (*10*), Ga^{69} (60.2%) and Ga^{71} (39.8%). The more abundant isotope captures a neutron to form 20-min Ga^{70}; the less abundant isotope captures a neutron to form 14.1-hr Ga^{72}.

$$Ga^{69} + n \rightarrow Ga^{70} \xrightarrow{20m} Ga^{70} + \beta^-$$

$$Ga^{71} + n \rightarrow Ga^{72} \xrightarrow{14.1h} Ga^{72} + \beta^-$$

The radiation characteristics of the radioactive products are described elsewhere (*13*).

The samples were transported to a position near the reactor tank of the pile and out again by means of an electronically controlled pneumatic tube device known as a "rabbit," which has been described elsewhere (*9, 15*). Samples ranging in weight between 0.3 and 0.5 g were cut from portions of meteorites free from discernible inclusions of troilite, silicate, or schreibersite. The samples were washed with 6*N* hydrochloric acid, distilled water, and alcohol to remove surface impurities. The samples were then placed in individual small plastic containers in the rabbit and irradiated for approximately 30 min. Standard samples of gallium 8-hydroxyquinolate were irradiated simultaneously. After removal from the pile, the samples were allowed to cool until the 20-min gallium activity had decayed. The unknowns and the standards were then chemically treated. In the case of the unknowns, the chemical procedure was designed to make use of the fact that gallium is ether-extractable, as the chloride (*5*), is amphoteric, and can be precipitated as the 8-

hydroxyquinolate. The combination of these chemical properties permits development of a procedure which successfully frees the gallium activity from other interfering activities.

TABLE 2

SUMMARY OF RESULTS ON CANYON DIABLO

Run no.	Gallium content (ppm)	Δ Deviation from mean
6	77.4	0.0
7	76.0	1.6
10	76.2	1.2
12	74.6	2.8
13	84.2	6.8
14	78.0	0.6
17	70.0	7.4
18	76.2	1.2
19	79.2	1.8
20	82.0	4.6
21	80.4	3.0
149	76.8	0.6
152	75.2	2.2
	Average: 77.4	

Standard deviation $\sigma = \sqrt{\frac{\Sigma\Delta^2}{n-1}} = 3.4$ (4.4%)

Precision $= \frac{\sigma}{\sqrt{n}} = \pm 0.9$

Final result for 13 runs: 77.4 ± 0.9 ppm

TABLE 3

SUMMARY OF RESULTS ON HENBURY

Run no.	Gallium content (ppm)	Δ Deviation from mean
42	15.2	1.6
43	15.1	1.7
44	15.9	0.9
51	18.4	1.6
52	17.8	1.0
53	17.9	1.1
59	16.7	0.1
61	15.2	1.6
62	15.6	0.8
158	18.2	1.4
159	18.2	1.4
	Average: 16.8	

Standard deviation $\sigma = \sqrt{\frac{\Sigma\Delta^2}{n-1}} = 1.3$ (8.0%)

Precision $= \frac{\sigma}{\sqrt{n}} = \pm 0.4$

Final result for 11 runs: 16.8 ± 0.4 ppm

Chemical Procedure for Gallium in Iron Meteorites: 1) Dissolve sample in hot concentrated hydrochloric acid in 50-ml beaker. Add 4 to 5 mg of Ga^{+3} carrier. Decant solution from any insoluble residue present (seldom more than 0.1% by weight). 2) Make solution 5.5 to 6.5 M in hydrochloric acid. Extract gallium with an equal amount of ether saturated with hydrochloric acid. Extract gallium from ether phase with water. 3) Repeat step 2. Boil ether from water phase. 4) Add sodium hydroxide until solution possesses a hydroxide concentration of 1 to 2 M, precipitating all ferric ion present. This precipitate brings down with it residual interfering activities.

TABLE 4

SUMMARY OF RESULTS ON ODESSA

Run no.	Gallium content (ppm)	Δ Deviation from mean
24	67.8	1.5
25	66.0	3.3
40	68.2	1.1
48	72.6	3.3
49	72.4	3.1
50	67.8	1.5
58	63.8	5.5
65	72.6	3.3
66	71.0	1.7
163	70.4	1.1
	Average: 69.3	

Standard deviation $\sigma = \sqrt{\frac{\Sigma\Delta^2}{n-1}} = 3.0$ (4.3%)

Precision $= \frac{\sigma}{\sqrt{n}} = \pm 0.9$

Final result for 10 runs: 69.3 ± 0.9 ppm

TABLE 5

SUMMARY OF RESULTS ON XIQUIPILCO

Run no.	Gallium content (ppm)	Δ Deviation from mean
26	56.2	1.0
27	51.4	3.8
28	59.3	4.1
32	53.0	2.2
33	54.6	0.6
34	54.8	0.4
35	53.0	2.2
36	54.2	1.0
37	51.6	3.6
146	65.0	9.8
155	54.5	0.7
	Average: 55.2	

Standard deviation $\sigma = \sqrt{\frac{\Sigma\Delta^2}{n-1}} = 3.9$ (7.1%)

Precision $= \frac{\sigma}{\sqrt{n}} = \pm 1.2$

Final result for 11 runs: 55.2 ± 1.2 ppm

Add one drop of aerosol, centrifuge, and discard the precipitate. Acidify the solution to a pH of 1.0 and heat to 60–70° C. 5) Add 5 ml of a 1% dilute acetic acid solution of 8-hydroxyquinoline. Add dropwise 3M ammonium acetate until the precipitation of yellow gallium 8-hydroxyquinolate is complete. 6) Filter and wash the precipitate with hot water, then ether. Determine the weight of the sample after heating at 110° C for 15 min. The sample is now ready to be counted.

Treatment of Gallium Standard. Samples contain-

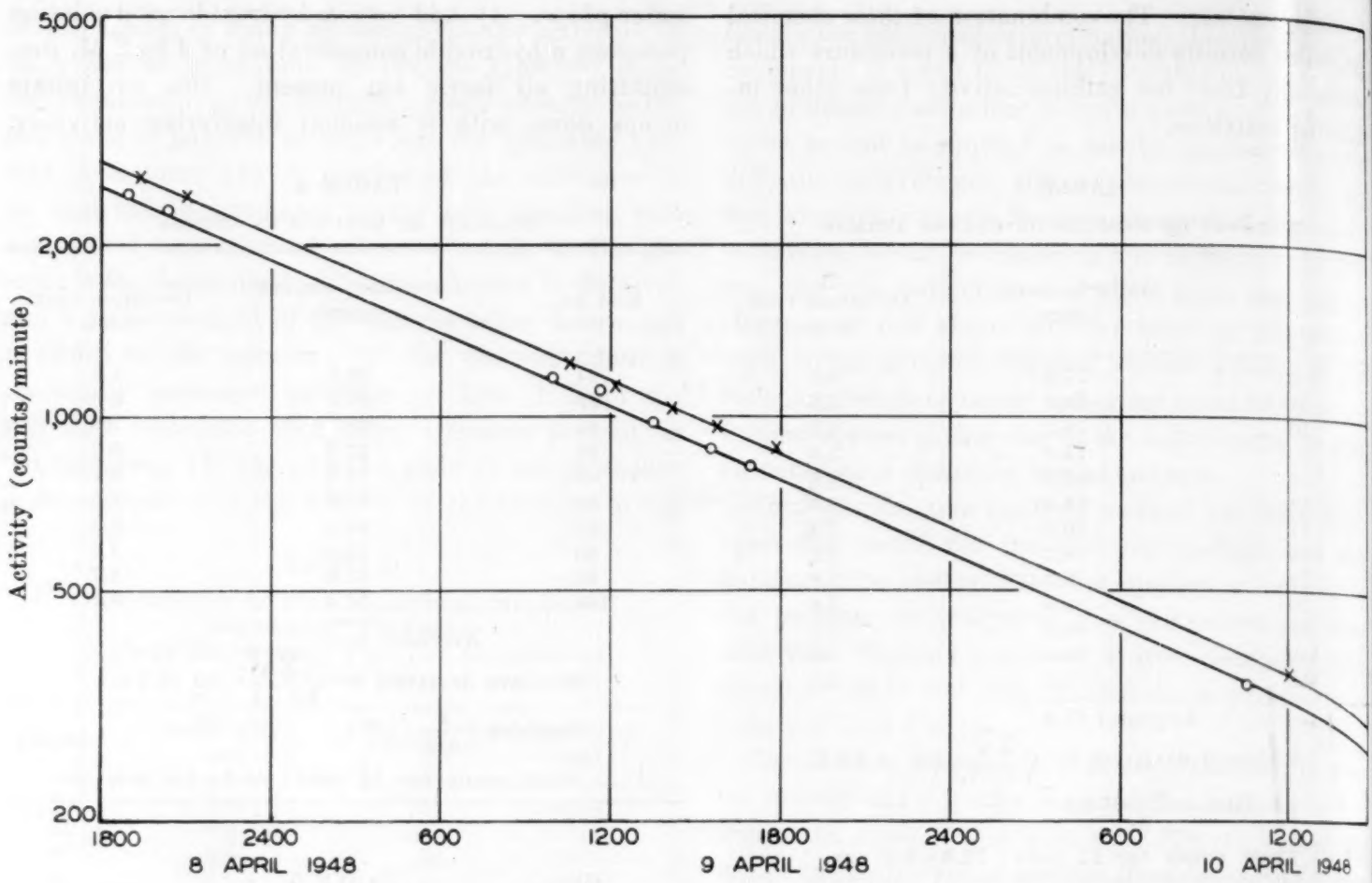

FIG. 1. Typical gallium decay curves. o Iron meteorite. × Standard.

ing approximately 10 mg of gallium 8-hydroxyquinolate were irradiated in containers identical with those used for samples of meteorites. The standards were dissolved in hot concentrated hydrochloric acid and diluted to 50 ml such that a 0.5-ml aliquot precipitated with gallium carrier as in the procedure above gave a dilution factor of 100 and the resulting precipitate had approximately the same counting rate as the gallium precipitate in the meteorite procedure.

Results. Extensive runs were made on four meteorites in order to ascertain the precision of the method. The results are shown in Tables 2, 3, 4, and 5. It will be noted that the standard deviation varies from 4.3% in the case of Odessa, where the gallium content is 69.3 ppm, to 8.0% in the case of Henbury, where the gallium content is 16.8 ppm. Such a drift of standard deviation with gallium content is to be expected under the conditions used, as all runs were made under nearly identical conditions of flux and irradiation time. Under such circumstances the counting rates for samples with low gallium content are lower than those with high gallium content. A marked increase of flux, irradiation time, or counting time would lower the standard deviation.

Figs. 1 and 2 show typical decay curves and aluminum absorption curves of standards and unknowns normalized to each other. Such data show that only gallium is being counted.

The results on Canyon Diablo, Henbury, Odessa, and Xiquipilco serve to show that the statistical errors involved in such a method of analysis are not prohibitively large. Runs were made on different days,

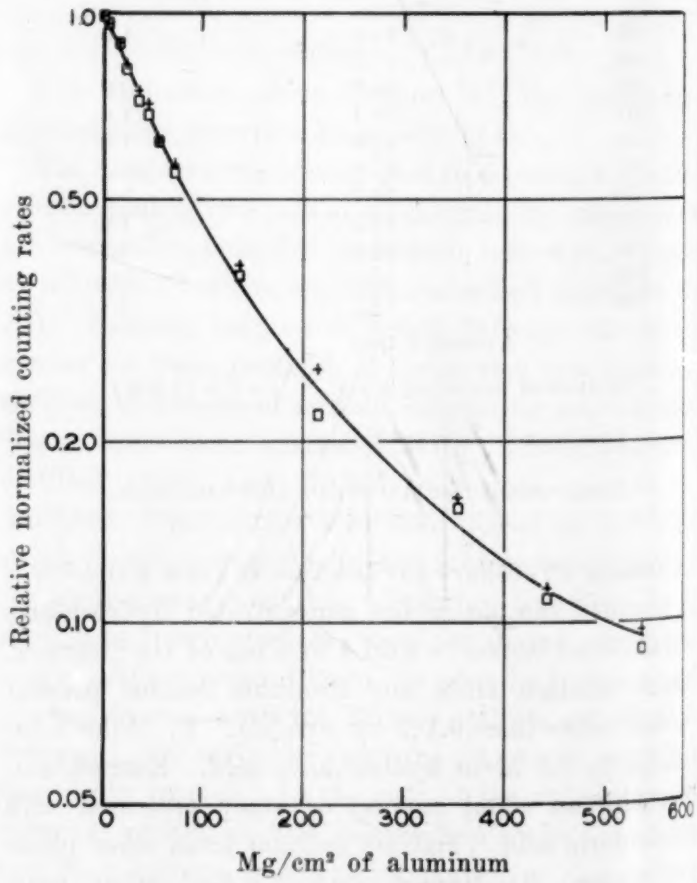

FIG. 2. Typical gallium absorption curves.

under varying conditions of neutron flux, location of samples in the rabbit, and irradiation time, and no constant drift of the results could be detected. However, if gallium in the form of room dust were being measured in addition to meteoritic gallium, a constant error would result. Consequently a number of substances were analyzed in order to ascertain whether or not the natural gallium contamination level was introducing errors. A sample of electrolytic iron, in which gallium could not be detected spectroscopically, was analyzed and found to contain 0.08 ppm of gallium. A sample of commercial aluminum was analyzed and found to contain less than 0.01 ppm of gallium. On the basis of these results, it seems safe to assume that no appreciable constant error due to gallium contamination was introduced in the measurements. The errors contributing to the standard deviation represent the sum of three effects: counting errors, actual deviations in gallium content from sample to sample (within a given meteorite), and actual errors involved in the chemical procedure.

A total of 14 iron meteorites were analyzed for gallium content. The results of the analyses are given in Table 6.

TABLE 6

GALLIUM CONTENT OF VARIOUS IRON METEORITES

Name	Number of runs	Average gallium content (ppm)
Arispe	5	64.1
Canyon Diablo	13	77.4
Canyon Diablo #2	5	85.0
Carleton	3	11.2
Deport	8	61.4
Henbury	11	16.8
Mount Joy	4	47.5
Odessa	10	69.3
Sandia Mountains	6	53.2
Spearman	6	21.4
Tlaxcala	2	20.8
Xiquipilco	11	55.2
Institute of Meteoritics #2	3	21.1
" " " #6	3	90.5

TABLE 8

SUMMARY OF PALLADIUM RESULTS ON HENBURY

Run no.	Palladium content (ppm)	Δ Deviation from mean
11	2.29	0.27
12	1.77	0.25
99	1.71	0.31
100	1.96	0.06
101	1.88	0.14
102	1.81	0.21
107	2.31	0.29
108	2.14	0.12
109	2.18	0.16
110	2.16	0.14
	Average: 2.02	

Standard deviation $\sigma = \sqrt{\frac{\Sigma\Delta^2}{n-1}} = 0.22$ (10.9%)

Precision $= \frac{\sigma}{\sqrt{n}} = \pm 0.07$

Final result for 10 runs: 2.02 ± 0.07 ppm

The Method Applied to Palladium. Palladium exists in iron meteorites to an extent of about 1 to 5 ppm. Activities obtainable in the rabbit were too low to permit the accumulation of precise enough data, and so all runs were made in the center of the pile, using irradiation times of approximately 1 hr. The element yields two prominent activities upon irradiation with slow neutrons, one of half-life 13 hr produced from Pd^{108} and one of half-life 26 min produced from Pd^{110}. The two isotopes giving rise to the activities have abundances of 26.8% and 13.5% re-

TABLE 7

SUMMARY OF PALLADIUM RESULTS ON CANYON DIABLO

Run no.	Palladium content (ppm)	Δ Deviation from mean
9	3.03	0.95
10	3.85	0.13
52	3.85	0.13
53	3.64	0.34
54	4.21	0.23
75	4.79	0.81
76	4.30	0.32
77	3.91	0.07
78	3.91	0.07
98	4.35	0.37
	Average: 3.98	

Standard deviation $\sigma = \sqrt{\frac{\Sigma\Delta^2}{n-1}} = 0.47$ (11.9%)

Precision $= \frac{\sigma}{\sqrt{n}} = \pm 0.15$

Final result for 10 runs: 3.98 ± 0.15

TABLE 9

SUMMARY OF PALLADIUM RESULTS ON ODESSA

Run no.	Palladium content (ppm)	Δ Deviation from mean
95	4.16	0.01
96	4.01	0.14
97	3.52	0.63
103	4.06	0.09
104	3.64	0.49
111	4.12	0.03
112	4.06	0.09
113	4.22	0.07
114	5.04	0.89
115	4.64	0.49
	Average: 4.15	

Standard deviation $\sigma = \sqrt{\frac{\Sigma\Delta^2}{n-1}} = 0.45$ (10.81%)

Precision $= \frac{\sigma}{\sqrt{n}} = \pm 0.14$

Final result for 10 runs: 4.15 ± 0.14

spectively (*13*). The radiation characteristics of the two activities are discussed elsewhere (*13*).

TABLE 10

SUMMARY OF PALLADIUM RESULTS ON XIQUIPILCO

Run no.	Palladium content (ppm)	Δ Deviation from mean
36	4.52	0.20
37	4.18	0.56
38	4.14	0.58
49	5.37	0.35
50	4.59	0.13
51	4.74	0.02
86	5.21	0.49
87	4.85	0.13
88	4.87	0.15
89	4.73	0.01
	Average: 4.72	

Standard deviation $\sigma = \sqrt{\frac{\Sigma\Delta^2}{n-1}} = 0.31$ (6.6%)

Precision $= \frac{\sigma}{\sqrt{n}} = \pm 0.10$

Final result for 10 runs: 4.72 ± 0.10

Samples of iron meteorite each weighing approximately 0.3–0.5 g were irradiated in soft glass vials, together with a standard of palladium dimethyl glyoxime. After irradiation the samples were permitted to cool until the 26-min activity had died away. The samples were then chemically processed. The chemical procedure used for the isolation of the palladium activity was a modification of a procedure developed by Seiler (*14*). Use was made of the fact that palladium can be precipitated as the dimethyl glyoxime, and that it also forms a complex in excess ammonium hydroxide.

TABLE 11

PALLADIUM CONTENT OF VARIOUS IRON METEORITES

Name	Number of runs	Average palladium content (ppm)
Arispe	4	2.69
Canyon Diablo	10	3.98
Canyon Diablo #2	3	5.30
Carleton	4	6.52
Deport	3	4.45
Henbury	10	2.02
Institute of Meteoritics #2	3	2.82
" " " #6	5	4.46
Mount Joy	3	3.30
Odessa	10	4.15
Sandia Mountains	3	2.24
Spearman	3	3.67
Tlaxcala	4	2.29
Willow Creek	3	3.70
Xiquipilco	10	4.72

Chemical Procedure for Palladium in Iron Meteorites: 1) Dissolve the sample of irradiated meteorite in hot concentrated hydrochloric acid in a 50-ml centrifuge tube covered with a watch glass. Add 10 mg of Pd^{+2} carrier. Keep tube in ice bath in order to inhibit oxidation of Fe^{+2}. (Palladium dimethyl glyoxime will not precipitate easily in the presence of Fe^{+3}.) 2) Add ammonium hydroxide until solution is 0.4 M in acid. Add 3–5 ml of 1% dimethyl glyoxime solution. Allow solution to stand 40 min.

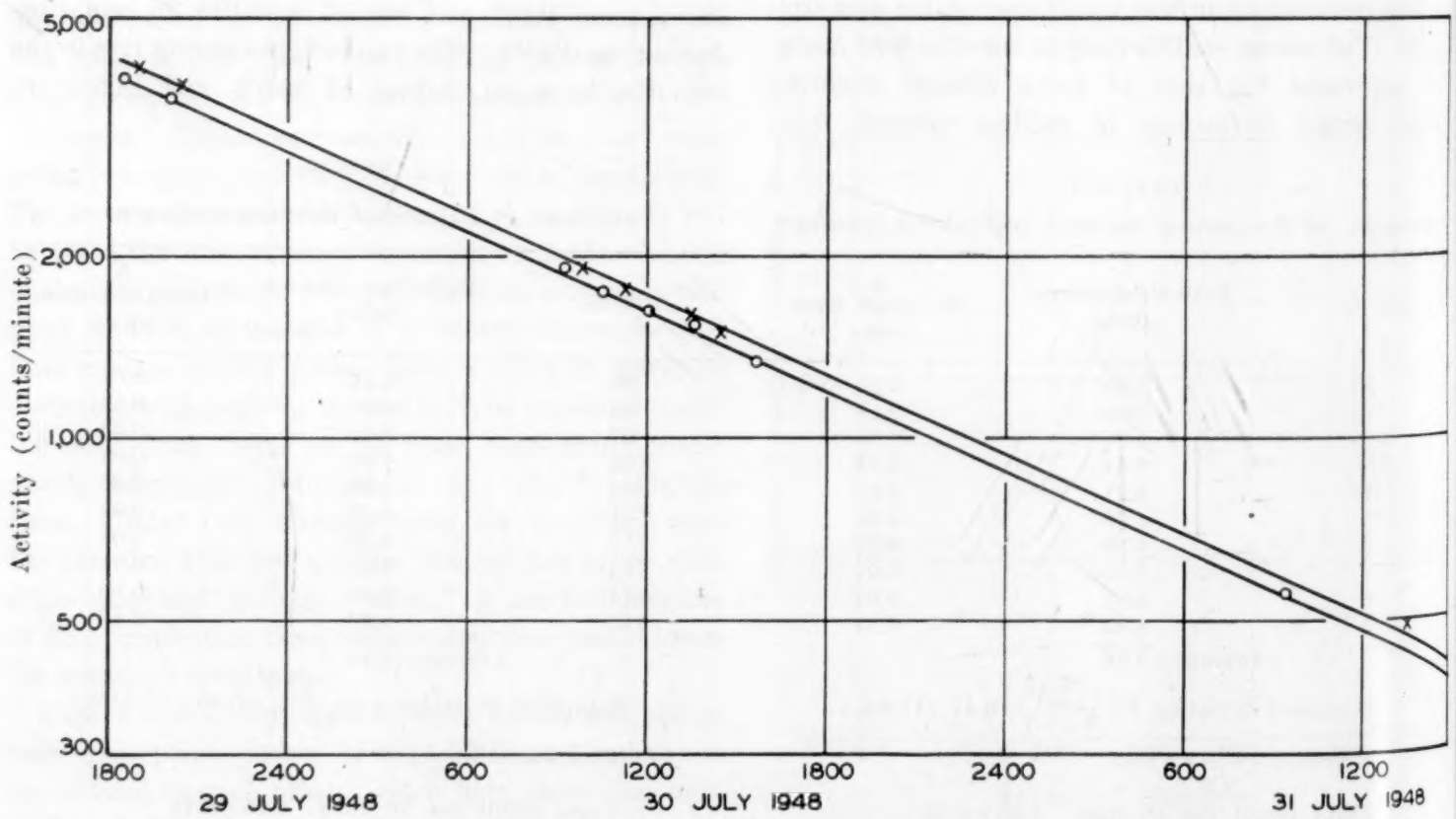

FIG. 3. Typical palladium decay curves. o Iron meteorite. × Standard.

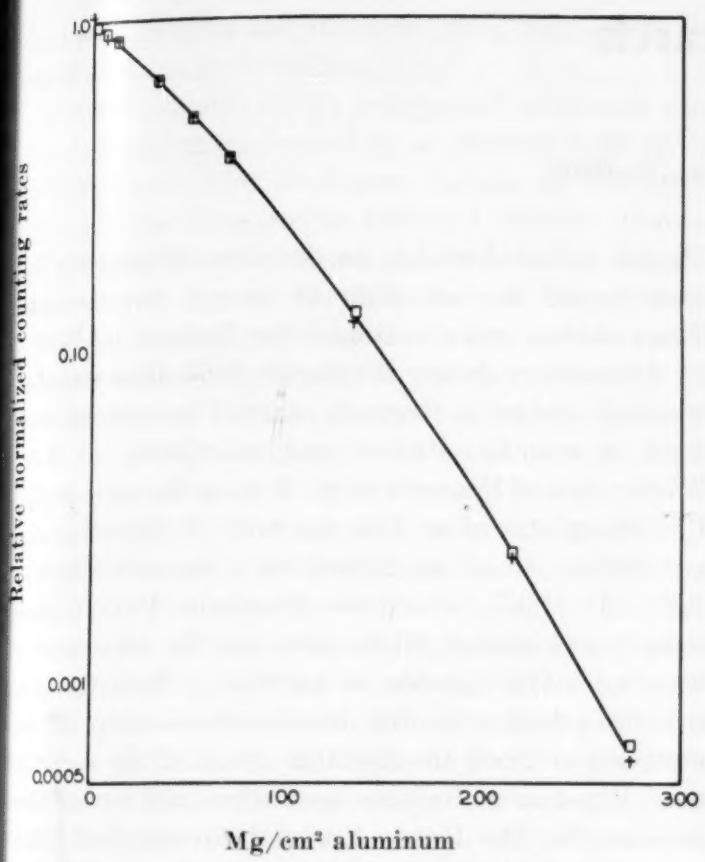

FIG. 4. Typical palladium absorption curves.
□Iron meteorite. + Standard.

Centrifuge. 3) Dissolve precipitate in 1 ml of hot concentrated nitric acid. Cool and dilute with 10 ml of water. Add 5 mg of Fe^{+3} carrier. Add excess ammonium hydroxide to precipitate iron. (This step removes a number of extraneous activities.) Add 10 mg of Ag^{+} carrier and enough iodide to precipitate all silver. (This step removes any silver activity present.) 4) Centrifuge and discard the precipitate. 5) Repeat steps 3 and 4. 6) Adjust acidity to 0.4 M. Centrifuge solution to remove any silver chloride precipitate formed. 7) Add 3–5 ml of 1% dimethyl glyoxime solution and allow solution to stand 40 min. Filter. 8) Wash the precipitate with first hot and then cold water and ethyl alcohol. Determine the weight of the sample after heating at 110° C for 10 min. The sample is now ready to count.

Treatment of Palladium Standard. Samples containing approximately 10 mg each of palladium dimethyl glyoxime were irradiated in containers identical with those used for meteorite samples. Each standard was then dissolved in hot concentrated nitric acid and diluted to 500 ml such that a 0.5-ml aliquot, when precipitated with the standard carrier aliquot, gave a dilution factor of 1 part per 1,000 and approximately the same counting rate as the palladium from the meteorite.

Results. In order to estimate the reproducibility and precision of the palladium procedure, as in the case of gallium, a number of runs were made on four meteorites. The results are shown in Tables 7, 8, 9, and 10. It will be noted that the standard deviations obtained are quite satisfactory. Table 11 gives the palladium contents of 15 iron meteorites. Figs. 3 and 4 show typical palladium decay curves and aluminum absorption curves.

Thus, the neutron pile as a tool in quantitative analysis is quite generally applicable and is particularly useful in analyzing unknowns for minor constituents. In applying the method to the problem of analyzing for minute concentrations of gallium and palladium in iron meteorites we found that the procedures gave consistent results, with low standard deviations from the mean. The procedures are not complicated, are free from interferences from other elements, and are also free from the danger of contamination during the course of the analysis.

Adapted from a paper presented at the Symposium on Nuclear Reactions held by the Division of Physical and Inorganic Chemistry of the American Chemical Society at Portland, Oregon on September 16, 1948. Submitted for declassification on August 16, 1948. Taken in part from a doctoral thesis to be submitted by Edward Goldberg to the faculty of the University of Chicago in partial fulfillment of requirements for the degree of doctor of philosophy.

References

1. BROWN, H., and PATTERSON, C. *J. Geol,* 1948, **56**, 85.
2. BROWN, H. *Sci. Mon.*, 1948, **68**, 383.
3. BROWN, H. *Rev. mod. Phys.*, in press.
4. GOLDSCHMIDT, V. M. *Geochemische Verteilungsgesetze der Elemente,* Oslo Norske Vaderskopr Acad.: 1937, **4**, Chap. 9.
5. GRAHAME, D. C., and SEABORG, G. T. *J. Amer. chem. Soc.*, 1938, **60**, 2524.
6. HEVESY, G. *Chemical analysis by X-rays and its applications.* New York: McGraw-Hill. 1932.
7. HEVESY, G., and LEVI, H. *Kgl. Danske Videnskab. Selskab, Math-fys. Medd.*, 1936, **14**, No. 5.
8. *Ibid.*, 1938, **15**, No. 11.
9. HUGHES, D. J., DABBS, J., CAHN, A., and HALL, D. *Phys. Rev.*, 1948, **73**, 111.
10. INGHRAM, M. G., HESS, D. C., BROWN, H. S., and GOLDBERG, E. *Phys. Rev.*, 1948, **74**, 343.
11. NODDACK, I. and W. *Naturwiss.*, 1930, **35**, 59.
12. SEABORG, G. T. *Rev. mod. Phys.*, 1944, **16**, 1.
13. SEILER, J. A. *Plutonium project report* 8.14.1, Vol. 9B. In preparation.
14. SUGARMAN, N. *J. chem. Phys.*, 1947, **15**, 544.

Seven Decades of Nutrition Research

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THE HUNDRED YEARS since the founding of the American Association for the Advancement of Science have been one of the most interesting half-centuries in the history of the world. In most fields of science the advances made during this period far overshadow the developments in any previous century. However, it is always valuable to review the early foundations upon which our modern science is built. Even in the field of nutrition, which is considered a 20th century development, we find many phases of it deeply rooted in the science of previous centuries.

There is no specific reason for starting my survey about 1880, although I was probably influenced by the statement in Richard O. Cumming's book, *The American and his food,* namely, "Few Americans thought about the chemical composition of foods before the last quarter of the Nineteenth Century. The diet reformers of the thirties had stressed the advantages of eating food in a condition approximating its natural state, but they were not analysts and had had little scientific data to substantiate their claims. Their teachings were largely forgotten by the eighties, though the word 'Graham' was still used to designate unbolted wheat flour."

Before proceeding to the laboratory developments of nutrition, I want to mention other factors which had much to do with the improved quality of food for the American people. For example, the availability of fresh foods, especially milk and meat, in cities, greatly increased upon construction of our railroads. Although the work of Koch and Pasteur, which indicated that every disease must have a positive causative agent, tended to retard the recognition of positive nutritional factors, the safeguarding of fresh foods from bacterial contamination, which became possible as a result of the early work in bacteriology, did much to improve nutrition in this country. Improved agricultural production also meant more food, but misguided attempts to purify our food products tended to overcome many of the advantages of increased production. The wheat bran and the meat scraps made better pigs and chickens, but the refined flour and the diversion of liver into animal feeds made poorer human beings.

Organized investigations in nutrition originated largely on the European continent and most of the work was closely allied with physiology. Voit at Munich initiated studies on the value of proteins but soon turned his attention to energy requirements. These studies were continued by Rubner in Berlin. In this country during the decade 1880–1890 Armsby, who had studied in Germany, carried on experimental work in animal nutrition and calorimetry at Yale, Wisconsin, and Pennsylvania. During the same period Chittenden started at Yale his work on digestion and metabolism, which continued until his retirement in 1922. In 1887, when the American Physiological Society was created, Chittenden was the only member who had a true interest in nutrition. Thus the contributions during the first decade were meager, but we must not overlook the fact that many of the Agricultural Experiment Stations were organized during this decade after the Hatch Act of 1887 and that much valuable nutritional work has come from these stations. When Babcock came to Wisconsin in 1887 he was convinced that other nutrients in foods besides carbohydrates, fats, proteins, and minerals were important.

The most important event during the second decade of our story, 1890 to 1900, is undoubtedly the work of Eijkman. On the basis of systematic experiments he was able to refute the theories that beri-beri might be due to the presence of pathogenic organisms in rice, to lack of mechanical stimulation of the intestine, or to insufficiency of total food. He suggested that beri-beri is a state of intoxication brought about by the metabolism of excessive quantities of starch and that the silver skin of the rice contains a substance which counteracts the toxic products of the disturbed metabolism. The conception of a positive factor in rice polishings, indispensable to health, did not develop until the following decade.

We are probably safe in concluding that no scientific studies on vitamins were conducted in the United States before the 20th century. However, during this last decade of the 19th century, Congress appropriated $10,000 for the year ending June 30, 1895 and $15,000 the following year to enable the Secretary of Agriculture "to investigate and report upon the nutritive value of the various articles and commodities used for human food." Atwater was placed in charge of nutrition investigations, and in 1896 Atwater and Woods published an extensive compilation on the proximate analysis of American food materials. This bulletin (No. 28) has been a standard reference on

food composition, and tables in many text books are based on these early values.

The next decade, or the first period in the new century, can be characterized by a growing interest in biochemistry. The American Society of Biological Chemists was organized in 1906 and both the *Journal of biological Chemistry* and the *Biochemical Journal* were started during the first part of the century. Lusk, an active member in the Society, continued to emphasize the importance of energy metabolism in both health and disease. Levine started his important work on nucleic acids and their breakdown products which are assuming such importance in nutrition at the present time. Folin and Benedict developed methods which could be utilized in studies on protein metabolism. The importance of amino acids, the constituents of proteins, in nutrition was being given consideration by Osborne and Mendel in this country, and Hopkins in England. Sherman, during his connections with the U. S. Department of Agriculture, established the early requirements for calcium, iron, and phosphorus in the human body. All of this work provided a sound foundation for future studies but did not stimulate any great interest in nutrition as such. The original Federal Food and Drug Act was passed during this period but the evolution of the law, which took place over a period of 25 years, was based largely on chemical analysis. Greatest emphasis was placed on adulteration of foods and drugs which could be recognized chemically. A few workers were beginning to recognize that true nutritional value of foods could be determined only by animal experimentation. The work of Eijkman was not too well known in this country, but Babcock and Hart were experimenting with calves on rations compounded according to available feeding standards.

The next decade, 1910–1920, brought an entirely new point of view. It was found that calves failed to grow on rations made entirely from products of the wheat plant but thrived on rations made from the corn plant. Hopkins obtained a very significant growth response in rats fed purified rations when a few cc of milk were added. The work of Osborne and Mendel, and McCollum and Davis showed that rats fed purified rations developed normally when the fats of the diet consisted largely of butter fat but failed when other fats, now known to be low in vitamin A, were used. Chicks grew normally if allowed access to sunlight shortly after hatching but developed severe leg weaknesses when they were hatched early in the spring. It was in 1914 that the Pellagra Commission reported that "Pellagra is in all probability a specific infectious disease communicable from person to person by means at present unknown" and that the Surgeon General of the U. S. Public Health Service ordered Dr. Goldberger to take charge of the pellagra investigations. Shortly thereafter, he produced typical pellagra in prison volunteers in Mississippi by placing them on a restricted diet, and also observed the development of blacktongue in dogs fed similar rations. During the first part of this period, Funk isolated a crystalline compound from concentrates which were active in the prevention of polyneuritis in pigeons. The substance which he actually isolated was nicotinic acid, which was later shown to be the antipellagra factor.

By the end of this decade, at least three separate vitamins were recognized as essential for the growth of young, and evidence was available which indicated that there might be additional vitamins. The real significance of these factors in total metabolism was unknown. With the outbreak of the first World War, attempts were made to utilize the limited knowledge available by advocating greater use of the so-called protective foods. This, together with the dramatic responses obtained upon supplying these foods when deficiencies occurred, led to the popularization of vitamins, which developed tremendously the next decade.

The period between 1920 and 1930 represents a transition stage between the early unstandardized animal studies and the more effective approach as a result of the greater interest which biochemists and organic chemists took in this field. By 1925 many laboratories were undertaking systematic nutrition studies, and fairly quantitative assay procedures were developed for the known vitamins. Even with these improved techniques and the use of more highly purified basal rations, many of the B vitamins were not recognized until the following decade, and apparently we still have some to look for. The relation of vitamin D to ultraviolet light was established in 1924, and this stimulated work on the chemical structure of sterols. The early recognition of the relationship of vitamin A to carotenoids stimulated studies on the structure of the carotenes, but the exact relationship was not established until 1929. Small amounts of crystalline vitamin B_1 were isolated in 1926, and in 1927 Szent-Gyorgi isolated a crystalline compound which King and co-workers later found to have anti-scorbutic activity. Before leaving this period, it is important to mention that the American Institute of Nutrition was organized in 1928. This society brought together a group of workers trained in many fields but with one common interest, and it also tended to balance the different phases of nutrition research.

The fourth decade of this century will undoubtedly be recognized as the period in history when greatest progress was made in the chemistry of vitamins and

other essential nutrients. Work on the isolation, characterization, and synthesis of vitamins has attracted the attention of many of the outstanding chemists in the world. The decrease in the wholesale price of most of the vitamins during the past 10 to 12 years is well known to all of us. It is needless to mention the significance, not only in nutrition but in all metabolic work, of the availability of sufficient quantities of these interesting chemical compounds to make their use unlimited. We are still looking for some of the new vitamins and as a new one becomes available progress accelerates in all phases of nutrition.

It was also in this decade that we began to study and appreciate the mechanisms through which the vitamins function in the living cell. In 1931 Peters, in England, showed that the brain tissue of thiamine-deficient pigeons was incapable of oxidizing glucose at a normal rate. This observation was soon followed by the demonstration that *in vitro* addition of thiamine to deficient brain tissue resulted in an increased rate of respiration. So today we think of thiamine in relation to the coenzyme decarboxylase, which is necessary in the metabolism of α keto acids, and of nicotinamide and riboflavin as necessary for the formation of enzyme systems which function in the transport of electrons during the oxidation of all types of foodstuffs. We think of the B_6 vitamins in relation to the metabolism of amino acids and pantothenic acid as a constituent of the coenzyme required for acetylations. Very recently it has been shown that one of the functions of biotin relates to the fixation of carbon dioxide with pyruvate to form oxalacetate. This relationship between vitamins and the prosthetic groups in enzymes makes it easy to understand the body's continuous requirement for vitamins, and the reason why vitamin requirement may vary, depending upon composition of the diet.

Furthermore, workers began to recognize the relation of vitamins to the growth factors for bacteria. The importance of riboflavin in the animal was recognized in 1933, and the need of this compound for the growth of lactic acid bacteria was shown in 1936. In 1937, nicotinic acid was shown to be important for both animals and microorganisms. Williams first recognized pantothenic acid as a growth factor for yeast in 1933; in 1939 this compound was shown to be the chick antidermatitis factor. Similar relationships were shown for pyridoxine, biotin, and inositol.

These studies led to the use of bacteria for the quantitative estimation of vitamins, and the first widely used method was that proposed by Snell and Strong in 1939 for riboflavin by means of *Lactobacillus casei.* However, extensive use of this and related methods did not take place until later.

The present decade has been most interesting to many of us. In the first place, we have seen the practical application of scientific knowledge to an extent which surpassed the hopes of the most enthusiastic workers. In November 1940 a committee, which later became the Food and Nutrition Board, was called together by the National Research Council to mobilize available knowledge of nutrition for the guidance of the several agencies of the Government which were facing problems involving food and nutrition. This group recognized immediately that if plans were to be made for securing optimum nutrition for either military or civilian groups, uniform values for human requirements must be established. The Board called upon everyone who had given any thought to this problem; and the dietary allowances, which are now so familiar, were first submitted to the National Nutrition Conference for Defense in May, 1941. These values have undergone several revisions and the new 1948 edition will soon be available.

In the words of Dr. Jeans "The allowances have potentialities for innumerable applications. Throughout the war they served as standards for the diets of our military forces throughout the world. The allowances are useful in making dietary surveys, in assessing the needs of our civilian population and as a guide in feeding population groups. They have been widely used as guides for family buying for welfare administration. They have been used as a basis in determining production goals. They serve as a focal point for guiding research that is to fill those gaps in our knowledge which are evident from a review of the derivation of the allowances."

It was also obvious that figures for dietary requirements were of little value unless the composition of the food products consumed was known with considerable accuracy. The need for such information became very critical during the war and in 1942 the Office of the Quartermaster General requested the Food and Nutrition Board to assemble, coordinate, and appraise the available data on food composition. The extensive tables resulting from these studies were finally published as U.S.D.A. Miscellaneous Publication No. 572. Work on the preparation of such tables did much to stimulate interest in the improvement and simplification of the assays for all the essential nutrients. As chemical and microbiological methods replaced animal assays, more and more evidence accumulated to show that many nutrients may be present in several different forms. For example, vitamin B_6 activity in foods may be due to the presence of pyridoxine, pyridoxal, or pyridoxamine. This merely emphasizes the complexity of biological material and the problems encountered when attempts are made

to place nutrition on a truly quantitative basis. The food industries and food processors have recognized this problem and have done much to support and stimulate work on food composition. This is important from their point of view since they must know the possible changes in nutritional value of foods during processing and cooking. Each nutrient and each of its different forms may be affected differently.

From these studies has come the interesting observation that often the availability of certain nutrients in natural foods may be improved by a proper degree of processing. Furthermore, natural foods can be improved by combining two incomplete food products or by adding minerals, synthetic vitamins, and even amino acids.

In an effort to bring national nutrition to the suggested levels of the allowances, the Food and Nutrition Board has recognized the desirability of limited types of food fortification. These include iodized salt; the addition of vitamin D to milk; the enrichment of flour, bread, and certain cereals with B vitamins and minerals; and the fortification of margarine with vitamin A. In applying these new scientific developments great care must be taken to control their use and to prevent the indiscriminate use of synthetic products to the detriment of the public. I believe the Council on Foods and Nutrition of the American Medical Association has made the most acceptable statement regarding fortification.

The Council wishes to encourage efforts to improve as far as possible the nutritive quality of all foods which contribute importantly to the American diet and which thereby constitute the food environment of the people. In spite of all these efforts there exists now and will undoubtedly continue to exist for some time, certain specific deficiencies in large segments of the population which can be remedied best through addition of indicated nutrients to cheap, staple foods that occupy substantial places in the dietary. The Council has favored and encouraged the addition of certain nutrients to selected foods for the purpose of overcoming these deficiencies by replacing as nearly as possible that which has been lost in processing, or by making appropriate foods serve as carriers of dietary essentials which are inadequately supplied by many diets. In any case, the purpose of adding synthetics to natural foods should be to prevent known deficiencies in groups of the population and not to use synthetic products which happen to be available at low cost.

The Council disapproves of unlimited or indiscriminate fortification of general purpose foods with minerals, vitamins, amino acids, or other nutrients.

Although fortification is largely a product of the present decade, it is important to mention that the addition of vitamin D to milk was initiated in 1928, and the program has now been in progress long enough to demonstrate its true value. The incidence of rickets in the children of this country is almost nil. Iodized salt was introduced still earlier but due to the absence of controlled procedures, the program has not been so successful.

The improved methods which have been used for the analysis of food have also been applied in metabolic studies especially in carrying out balance studies and saturation tests. These procedures have done much to improve the diagnosis of early nutritional deficiencies. They have also stimulated direct studies on human subjects. For example, studies at the Elgin State Hospital have been in progress several years to determine possible variations in the thiamine and riboflavin requirements between young and old subjects.

Another great development, which will be given more and more recognition with time, was the establishment of the Food and Agriculture Organization of the United Nations, and the recognition that human nutritional needs can only be satisfied through a sound food policy which is not only national but international. It is most gratifying that these applications of science have not detracted from fundamental studies. For example, much of the work on isolation, characterization, and synthesis of folic acid was done during the war period. The availability of folic acid makes it possible to continue the search for remaining members of the vitamin B complex. Although folic acid may not be directly concerned with pernicious anemia, the work on folic acid led to the final isolation of vitamin B_{12}, which appears to be the true pernicious anemia factor. In other words, these studies clear up problems which were initiated two decades ago, when Minot and Murphy found liver and liver extract to be effective in pernicious anemia.

It is also apparent that some of the newer nutritional factors are active in extremely small quantities. For example two to five micrograms of vitamin B_{12} are sufficient to give a very significant hematopoietic response in pernicious anemia. The daily requirement for the human is probably much less. This brings us to another very interesting development which has taken place largely during the present decade, namely the significance of the intestinal microflora in nutrition. I cannot help but refer to the first experiment conducted in our laboratory back in 1940, when it was shown that the feeding of sulfaguanidine reduced the growth rate of rats and that this retardation could be overcome with liver preparations, because many of my co-workers were skeptical when I explained the results on the basis of retarded intestinal synthesis of unknown B vitamins. Today we

recognize the importance of intestinal synthesis of vitamins and possibly other nutrients not only in animal experiments but in human nutrition. Emphasis is being placed on the relation of intestinal flora to conditioned deficiency diseases in man.

It will not be possible for me to give any extensive review of the many important fundamental problems now under investigation, but I shall mention a few.

The studies on amino acids initiated 40 years ago are now being brought to successful conclusion. Rose has made extensive studies with humans to determine the quantitative requirements of adults. Cannon has also shown that the recognized essential amino acids may suffice for the maintenance of nitrogen equilibrium in adult rats. However, recent work in our laboratory with the growing animal indicates that many of the nonessential amino acids also need to be added for optimum growth. Very recently we have secured growth in mice equal to that obtained with intact protein by supplying all the amino acids in free form.

Another problem is the interrelationship between various nutrients—the most interesting of which is the interrelationship between niacin and tryptophan. This has led to the complete understanding of the early work of Goldberger during the second decade of this century. Today we know definitely that pellagra is associated with corn consumption not only because it is low in niacin but also because the protein in corn, zein, is low in the amino acid tryptophan.

One of the most interesting developments during this decade has been the recognition of metabolic antagonists. The availability of many of the nutrients in pure and synthetic form has allowed modification in the structure of these compounds. Out of this work has come the general recognition that slight modifications in the structure of certain vitamins may change them from essential nutrients to detrimental metabolites. Although these observations may not have direct application to nutrition, because few of the antagonists occur in nature, these relationships will give much information regarding metabolism.

All of this work emphasizes the importance of recognizing all the nutrients taken in by living cells, whether they be present in animals, plants, or microorganisms. These nutrients may not always be essential, but they may become important under certain environmental conditions. There is great hope for the future in nutrition, if we recognize this broad principle, and if we continue to develop techniques which will measure some of the nutrients which are active in the minutest quantities. During the past few decades, we have developed from a point where we thought milligram quantities were important to a point where we must recognize microgram and millimicrogram quantities. If we can supply these substances in optimum amounts and in the proper ratios we will have an efficient machine for the utilization of energy for growth and development, or in other words, we will have optimum health. In spite of the tremendous advances in the science of nutrition and in food technology, our world food problem today is still one of total calories. On the other hand, in areas like the United States where caloric undernutrition has been relatively rare for many years, there appears to be some correlation between the increased incidence of degenerative diseases and high caloric intake, and efforts are under way to control food intake at least to a limited extent.

We can therefore look back on seven decades of nutrition research with considerable satisfaction. Enthusiasm over newly discovered nutrients may have given too great emphasis to certain phases of nutrition for short periods of time, but active workers soon reinstituted the proper balance. Workers in nutrition have made use of the scientific advances in many of the related fields, and at the same time have contributed to the advances in allied fields, but in doing so they have not diverged too far from the main goal of optimum health for all.

Based upon an address presented at the Symposium on Food and Nutrition, American Association for the Advancement of Science, Washington, D. C., September 16, 1948.

References

1. CHITTENDEN, RUSSELL H. *The development of physiological chemistry in the United States.* New York: Chemical Catalog Co., 1930.
2. CHITTENDEN, RUSSELL H. *The first twenty-five years of the American Society of Biological Chemists.* Baltimore: Waverly, 1945.
3. ELVEHJEM, C. A. "Biological Significance of Vitamins," and Folkers, Karl, "Some Aspects of Vitamin Research" in *Currents in biochemical research,* edited by D. F. Green. New York: Interscience, 1946.
4. ELVEHJEM, C. A. *J. Amer. diet. Ass.,* 1948, **24**, 653.
5. ELVEHJEM, C. A. *Fed. Proc.,* 1948, **7**, 410.
6. EVANS, E. A., JR. (Ed.). *The biological action of the vitamins.* Chicago: Univ. Chicago Press, 1942.
7. GOLDBERGER, J., and WHEELER, G. A. *Public health report* 30, p. 3336, 1915.
8. HART, E. B., MCCOLLUM, E. V., STEENBOCK, H., and HUMPHREY, G. C. *Wis. agric. exper. Sta. Bull.* 17, 1911.
9. MCCAY, CLIVE M., and TODHUNTER, E. NEIGE. *J. Amer. diet. Ass.,* 1948, **24**, 737.
10. *Recommended dietary allowances.* Series No. 126. Washington D. C.: National Research Council, October 1948.
11. SCHULTZ, T. W. (Ed.). *Food for the world.* Chicago: Univ. Chicago Press, 1945.
12. "Symposium on Applications of the Newer Knowledge of Nutrition to Present Day Problems." *Fed. Proc.,* 1946, **5**, 267.
13. WOOLEY, D. W. *Phys. Rev.,* 1947, **27**, 308.

TECHNICAL PAPERS

The Prevention and Treatment of Motion Sickness I. Seasickness[1]

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During the year 1947, Dramamine (β-dimethylaminoethyl benzohydryl ether 8-chlorotheophyllinate) was sent by the manufacturer to the Allergy Clinic of the Johns Hopkins University and Hospital for experimental investigation of its value in the control of the symptoms of hay fever and urticaria. The drug was administered to a pregnant woman who complained of urticaria and who incidentally has suffered all her life from car sickness. Unexpectedly, the car sickness was relieved as well as the urticaria. It was possible to control the car sickness of this patient at will. A placebo failed repeatedly, but the drug Dramamine gave her complete relief if she took 50 mg a few minutes before she boarded the streetcar.

A study of seasickness was planned and executed on the U. S. A. T. "General Ballou." This transport carried 1,366 soldiers to Bremerhaven, Germany. The voyage began on November 27, 1948 and, after a rough passage, terminated on December 7, 1948. Complete cooperation was given by the Surgeon General's office and by the Transport Command. Four adjacent compartments on the transport were set aside for the controlled study of the 485 men who were assigned to them and subjected to the same motion of the sea. Treatment was planned so that half the men were given Dramamine or a placebo of lactose at the time of departure from New York Harbor; the other half were given Dramamine or a placebo 2–12 hr after the onset of symptoms of seasickness. Adequate control groups were given a placebo. The dose of Dramamine was 100 mg every 5 hr and before retiring. Dramamine prevented seasickness in all but two of the 134 men who occupied compartment 3-E; a placebo failed to relieve the symptoms in all controls who developed true seasickness in compartment 3-F. However, the control group (34 men) obtained complete relief of symptoms within 1 hr after the first dose of Dramamine was administered. The drug gave complete relief to 14 men in compartment 4-E who developed symptoms 3 hr or more after the transport left New York. A placebo failed to relieve 14 men in compartment 4-F, but these men obtained complete relief ½ hr after Dramamine was substituted for a placebo. Nineteen men who developed symptoms (nausea and dizziness) 3 hr or more after the transport left New York were relieved by a placebo. These men required no medication during the last seven days of the voyage to Bremerhaven. Among 881 men who occupied other compartments on the transport, 195 cases of severe seasickness developed. Of these, 187 derived complete relief ½ hr after the administration of Dramamine. Relapses were induced by the substitution of a placebo, but these symptoms were relieved within ½ hr after the administration of Dramamine. During a period of 10 days, Dramamine was given to 389 cases of seasickness. Of this number, 372 were completely relieved of symptoms within 1 hr after the first dose of 100 mg. Seventeen cases derived only partial or no relief. A dose of 100 mg prescribed every 5 hr and before retiring was adequate to control the most distressing symptoms. When the patient was unable to retain a capsule administered orally, he did retain and absorb the drug given rectally. The benefit derived by this method was as rapid and as complete as that derived by the oral method. No reaction to Dramamine was encountered by any soldier to whom it was administered during the period of 10 days.

[1] This investigation was made possible by the Chief of Staff and the Surgeon General of the United States Army.

[2] The authors wish to express their appreciation to the Transport Command, especially Major C. W. Hodges, Lt. J. L. Soelling, and the nurses of the U. S. A. T. "General Ballou"; and to G. D. Searle & Co., of Chicago, who prepared the Dramamine and the placebo for the investigation.

The Effectiveness of Dramamine in the Prevention of Airsickness

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The recent report by Gay and Carliner (*2*) on the effect of the new antihistaminic drug, Dramamine (β-dimethylaminoethyl benzohydryl ether 8-chlorotheophyllinate), as a preventive and treatment for seasickness has attracted widespread attention. Investigations on motion sickness in the past have shown a paucity of controlled studies carried out on shipboard or on aircraft. The methodology utilized by Gay and Carliner is strikingly provocative in that practical studies on motion sickness under actual precipitating conditions were subjected to controlled scientific scrutiny.

Armstrong (*1*) has pointed out the dearth of comprehensive reports in the literature on the subject of motion sickness caused by aircraft in flight. This form of motion sickness is well known and is encountered often enough to be considered a major problem of aviation medicine. Air sickness is one of the most frequent

causes of distress among airline passengers. In military aviation an appreciable number of flying cadets are eliminated for this reason; it is not unusual for combat aircrews to be affected; and not infrequently a high percentage of airborne troops and paratroopers are more or less incapacitated by the time they have reached their destination.

Smith (*3*) in 1946 reviewed all of the previous work aimed at finding a motion sickness remedy and recommended that until a better drug was available hyoscine hydrobromide be used in the prevention of airsickness in Air Force personnel. The reported remarkable effectiveness of Dramamine (*2*) in the prevention and treatment of seasickness would indicate that this drug might also be valuable in airsickness and in February 1949 the Air Surgeon authorized the USAF School of Aviation Medicine, Randolph Air Force Base, Randolph Field, Texas, to initiate tests.

A preliminary controlled study has been completed. A procedure was devised whereby one-hour flights simulating flight through turbulent air in a C-47 (DC-3) airplane were utilized. Volunteers were obtained from among individuals stationed at Randolph Air Force Base who were not on flying duty. No other selection factors were utilized within this group since it was desired to have as a test group a cross-section of young adult males who had not become conditioned or adapted to aircraft motion. In view of this it can be considered that the individuals studied are similar to those studied by Gay and Carliner.

Twelve flights of 18 individuals each have been carried out to date. On each flight conditions encountered in flying through gentle and moderately turbulent air were simulated. All variable factors were either controlled or "randomized." Methodology was as follows:

(a) Each group of 18 men on a flight was subdivided into a group of nine who received a 100-mg tablet of Dramamine and another nine who received a placebo identical in appearance. Care was taken to prevent each individual from knowing whether he received drug or placebo.

(b) The drug or the placebo was administered concurrently from 25 to 45 min before each flight.

(c) Seating arrangement in the airplane was carefully controlled in that an equal number of individuals who received the drug were distributed symmetrically in the forepart and the afterpart of the cabin. The same procedure was used in seating the individuals who received the placebo. In addition, drug and placebo subjects were symmetrically distributed on the right and left sides of the cabin.

(d) All flights were made at an altitude of 5,000 feet above mean sea level. The pilots had previously developed methods of simulating flight through gentle and moderately turbulent air. These maneuvers may be summarized as follows: (1) Yawing or "fish-tailing"—produced by moving the rudder from side to side. (2) Rolling—produced by raising and lowering the wings alternately by the aileron controls. (3) Pitching (including ascending)—produced by moving the elevators causing up-and-down motion. Minor altitude variations were obtained similar to those caused by updrafts and downdrafts. (4) Various combinations of the foregoing maneuvers were used and approximately three-fourths of the duration of each flight was devoted to intermittent simulation of flight through turbulent air.

(e) As in previous studies carried out on motion sickness at the School of Aviation Medicine, the incidence of airsickness in the subjects was judged on a purely objective basis, i.e., whether or not vomiting occurred.

Twelve flights were made under the conditions described and a total of 216 subjects were tested. One-half of the subjects received Dramamine and the other half a placebo. The results are shown in Table 1.

TABLE 1

Preflight medication	Airsick		Not sick		Total number
	Number	Percentage	Number	Percentage	
Dramamine ..	31	28.7	77	71.3	108
Placebo	60	55.6	48	44.4	108

Under the conditions described above 28.7 percent of those given Dramamine became ill as opposed to 55.6 percent among those given a placebo. Application of the statistical technique known as sequential analysis to the results shown in Table 1 indicates that additional experimental flights as described above would result merely in further verification of the same relative difference of incidence of airsickness.

So important is the solution of the problem of motion sickness in both commercial and military aviation that any drug or type of drug which appears to have significant effects in preventing airsickness warrants extensive investigation. Although the results of this experimental study are not spectacular, Dramamine appears to decrease the incidence of airsickness. More exhaustive studies under actual turbulent conditions are indicated. Additional research is presently under way at the USAF School of Aviation Medicine concerning the mechanism of action of Dramamine and other drugs in the prevention and treatment of airsickness.

References

1. Armstrong, Harry G. *Principles and practice of aviation medicine*, (2nd ed.) Baltimore: Williams and Wilkins, 1943.
2. Gay, Leslie N., and Carliner, Paul E. "The Prevention and Treatment of Motion Sickness, I—Seasickness." Presented before the meeting of the Johns Hopkins Medical Society, Feb. 1949.
3. Smith, Paul K. "Present Status of Drugs for Use in Motion Sickness with Particular Reference to Airsickness." USAF School of Aviation Medicine Research Project 468, report No. 1, June 14, 1946.

Chronic Toxicity of Gossypol[1]

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The widespread publicity attained by gossypol as an appetite depressant, since the report (*3*) that highly purified preparations of gossypol act by delaying the passage of food from the stomach to the duodenum in the rat, has led to repeated requests for the use of this material for clinical trial in the treatment and control of obesity. Gossypol, a polyphenolic yellow pigment, is the principal component found in the pigment glands of cottonseed (*1*). Its acute oral toxicity and that of cottonseed pigment glands for rats, mice, rabbits, and guinea pigs have been reported (*2*).

To determine the effects of repeated oral doses of gossypol on the food intake and body weight, four young, litter-mate male dogs (5.0 to 5.4 kg) were given daily doses of 0, 50, 100 and 200 mg/kg body wt of the material, respectively, during three different experimental periods according to the following schedule: 55-day control period, 5-day experimental period (gossypol by capsule), 9-day control (rest) period, 5-day experimental period (gossypol by stomach tube), 9-day control period, 9-day experimental period (gossypol by stomach tube). From the first administration to the last, each of the three experimental dogs received a total of 19 daily doses of gossypol within a period of 37 days, which resulted in the death of all three dogs within 5 days after the last dose (one on the fourth and two on the fifth day).

The consistent effects of repeated doses of gossypol in the dogs were nausea, vomiting, diarrhea, anorexia, and marked weight loss. During the final period of gossypol administration the average food intake (dry basis) of each of the experimental dogs fell to 6.0, 0.4, and 3.0 g/kg body wt/day, respectively, while the control dog ate 28.0 g/kg body wt/day, and they lost 20, 26 and 25% of their body weight (the control dog lost 0.7%) within a period of 9 days. Post-mortem examination showed essentially the pathological findings reported for the rat, mouse, rabbit, and guinea pig (*2*), with marked lesions of focal necrosis involving the cecum, ileo-cecal valve, and adjacent portions of the large intestine. Further experiments are in progress.

It is suggested that the use of gossypol in human subjects be withheld until more data on its pharmacology and toxicology are available.

References

1. Boatner, C. H., Hall, C. M., O'Connor, R. T., and Castillon, L. E. *Bot. Gaz.*, 1947, **109**, 108–120.
2. Eagle, E., Castillon, L. E., Hall, C. M., and Boatner, C. H. *Arch. Biochem.*, 1948, **18**, 271–7.
3. Zucker, T. F., and Zucker, L. M. Abstracts of Papers, Amer. Chem. Soc., April, 1947, p. 47B.

[1] The samples of gossypol used in this study were supplied by the Southern Regional Research Laboratory, U.S.D.A., New Orleans, Louisiana, one of the laboratories of the Bureau of Agricultural and Industrial Chemistry, Agricultural Research Administration.

Application of Chromatography to the Separation of Subcellular, Enzymatically Active Granules

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It has recently been shown (*3*) that the chromatographic columnar adsorption method (*4, 6*) can be applied to the partial separation of biologically active particulates of virus dimensions from a chicken tumor extract. The present communication extends this chromatographic application to larger subcellular components, in the microscopically visible range, as found in pigmented mammalian tumors.

It has been found that melanized granules, varying in size from 0.2 to 0.6 μ or more, of the Cloudman S91 and Harding-Passey mouse melanomas, can be reversibly adsorbed on Celite columns (Fig. 1) and are thus subject to chromatographic manipulation. As a consequence, certain other constituents of the tumor homogenates employed as starting material can be readily separated from the granules, thereby providing a basis for noncentrifugal segregation of a substantial portion of the other tissue components. The particulate elements (*1, 2, 5*) separated by chromatography were found to possess high dopa oxidase and succinoxidase activities. As indicated by the

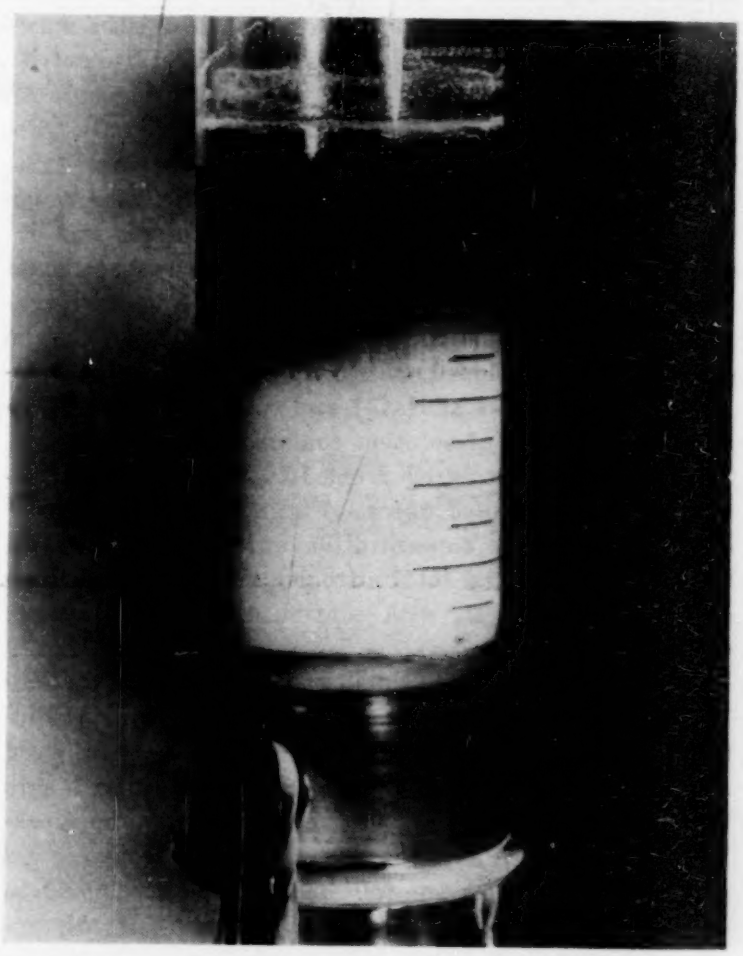

Fig. 1.—Adsorbed melanin granules on the developed chromatographic column prior to extrusion and segmentation.

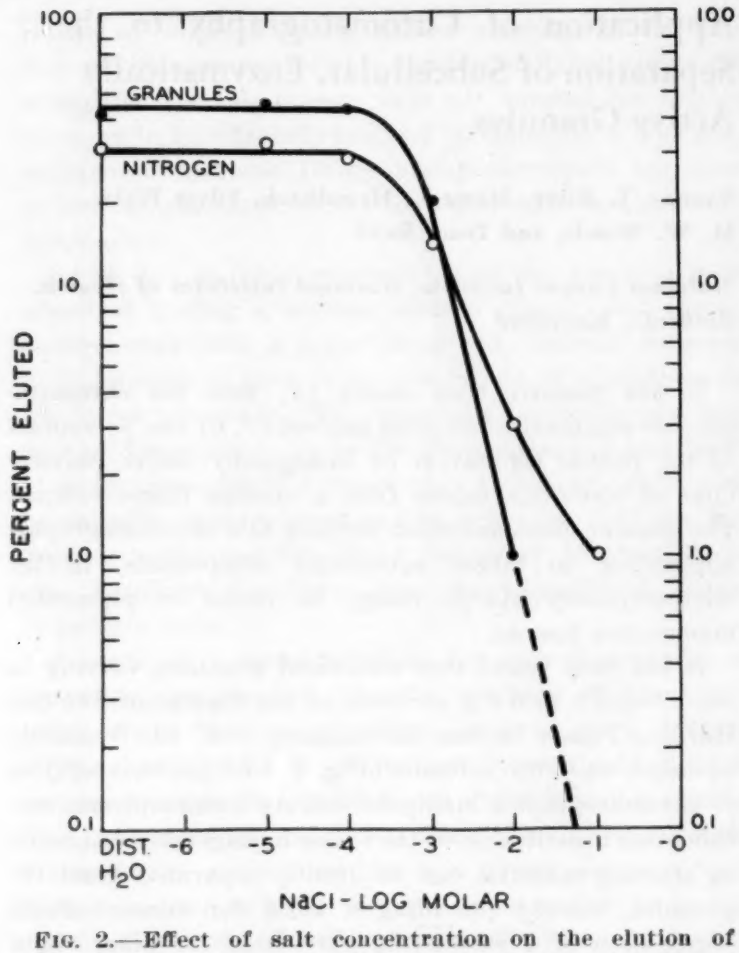

FIG. 2.—Effect of salt concentration on the elution of melanized granules and total nitrogen following the adsorption of equal quantities of a partially purified suspension on separate columns.

data below, granules so isolated possessed comparable or higher activities per unit of nitrogen than did the starting material, which had been partially purified by centrifugation, and considerably higher activities per unit of nitrogen than the starting extracts, where only preliminary centrifugal purification was employed.

In order to determine the adsorption and elution range of S91 melanin granules in this system, a curve was obtained by adsorbing from physiological saline equal quantities of granules (partially purified by centrifugation) on six identical 8×35 mm microcolumns. The columns were developed with 5 ml of additional physiological saline (0.154 M NaCl) and each column was then eluted with 10 ml of solution containing various concentrations of NaCl ranging from 10^{-1} to 10^{-6} M, and terminating with distilled water. Fig. 2 shows the influence of sodium chloride concentration on the elution of the melanin granules and total nitrogen, and indicates strong adsorption at 0.1 M, with continued influence through 0.001 M.

The percent granules eluted was estimated by measuring the optical density of the eluate at 650 mμ. A dilution curve of the centrifugally purified granules followed Beer's law, giving a straight line relationship with a zero intercept. Total nitrogen was determined by the Koch-McMeekin micro-Kjeldahl method,[1] and the enzymic activity of the granules was followed by their succinoxidase values determined manometrically in the Warburg apparatus. The pH of all solutions, including the tumor extracts, ranged from approximately 6.5 to 7.5. Within these limits, pH has little influence on adsorption or elution compared with the effect of salt concentration. In general, the adsorption and development procedures were carried out with cold solutions (2° to 10° C), while the elution was done with solutions at room temperature. The microcolumns were packed by introducing 5 ml of a 10% slurry of #503 Celite over a plug of absorbent cotton.

After establishing conditions for adsorption, development, and elution of the granules, the following experiment with a larger column was performed. Forty ml of a crude 20% S91 tumor extract[2] in saline was adsorbed on a dry Celite column 34×40 mm. A black zone of melanin granules formed in the upper part of the column and a pink zone containing hemoglobin and other tissue components developed immediately beneath the granules and migrated into the filtrate just behind a colorless zone of solvent. The column was developed with 40 ml of cold 0.154 M NaCl (0.9%), which was collected in the filtrate together with the pink fraction.

The moist column was extruded and cut into eight 5-mm segments, as illustrated in Fig. 3. In view of the adsorption-elution results shown in Fig. 2, each segment was separately eluted with distilled water, and the eluate tested for turbidity, succinoxidase activity, and nitrogen. The results are shown in Table 1 and Fig. 3. The data show that the granules were retained and subsequently eluted from the upper part of the column, while the preponderance of the starting nitrogen migrated into the percolate. This resulted in a more than 6-fold purification of the granules, as demonstrated by the relative increase in the succinoxidase $QO_2(N)$ value of fraction 2 compared with that of the starting material. The percolate (fraction 10), showed a corresponding decrease in activity, as did fractions 7 through 9. This adsorption behavior is similar to that found for the virus-like agent of chicken tumor I (3). The eluted particulate fraction 2 had a high population of melanized granules 0.3–0.6 μ in diameter, which were easily visible in the ordinary light and phase contrast microscopes.

If the above procedure is modified so that the elution is done by flowing chromatography rather than extrusion and segmentation, one black zone migrates down the column at a much faster rate than another, so that two distinct zones occur. While this indicates a chromatographic difference, or a change in a portion of the granules, the physiological or chemical differences of the two zones are yet to be studied. In experiments where this zone is left on the column it is expressed as elution inefficiency, as indicated in Fig. 2 and Table 1.

The association of the enzyme activity and the observed granules was attested by the fact that secondary

[1] Determined in Mr. Charles A. Kinser's laboratory, National Institutes of Health.

[2] This extract was prepared by grinding the tumor tissue at 1°–5° C with 0.9% NaCl to make a 20% homogenate. This was centrifuged for 3 min at approximately 1,000 x gravity, the supernatant was poured off, and its volume adjusted with saline to reestablish the original volume and yield a 20% saline extract. Such extracts contained most of the melanin granules, together with some nuclei and other coarse particulate matter.

centrifugation of such eluates at speeds just sufficient to sediment most of the particles yielded a fraction with succinoxidase $QO_2(N)$ values equal to or higher than the whole eluates. The same was also true for the dopa oxidase activity of the sedimented particles although, in contrast to succinoxidase, substantial quantities of dopa oxidase were also found in the saline and distilled water supernatants. Table 2 presents some of the dopa oxidase activities obtained when employing flowing chromatography. Further details concerning the different behavior of these two enzyme systems when manipulated chromatographically will be described elsewhere.

TABLE 1

RELATIVE DISTRIBUTION OF MELANIZED GRANULES, SUCCINOXIDASE ACTIVITY, AND TOTAL NITROGEN IN THE COLUMN ELUATES FOLLOWING THE ADSORPTION OF 40 ML OF A CLEARED TUMOR EXTRACT, AND DEVELOPMENT WITH AN EQUAL VOLUME OF 0.9% SALINE

Fraction	Oxygen consumption		Nitrogen		$QO_2(N)$		Optical density	
	µl/hr/ml	%	mg/ml	%	µl O_2/hr/mg N	%	D at 650 mµ	%
1. Starting extract*	16.7	100.0	1.48	100.0	11.3	100.0	1.40	100.0
2. Top 5 mm of column†	13.1	78.4	0.18	12.2	72.8	644.2	0.80	57.1
3. 2nd 5 mm of column	2.8	16.8	0.11	7.4	25.5	225.7	0.32	22.8
4. 3rd 5 mm of column	0.9	5.4	0.07	4.7	12.9	114.1	0.24	17.1
5. 4th 5 mm of column	1.5	9.0	0.07	4.7	21.4	189.4	0.20	14.3
6. 5th 5 mm of column	1.6	9.6	0.06	4.0	26.7	236.3	0.14	10.0
7. 6th 5 mm of column	0.2	1.2	0.052	3.5	3.8	33.6	0.09	6.4
8. 7th 5 mm of column	0.2	1.2	0.048	3.2	4.2	37.2	0.08	5.7
9. 8th 5 mm of column	0.3	1.8	0.062	4.2	4.8	42.5	0.07	5.0
10. Percolate‡	2.1	12.6	1.13	76.4	1.9	16.8	0.10	7.1

* See text footnote 2.
† All column segments eluted with 10 ml of solution, or ⅓ the original volume of extract introduced on the column.
‡ Calculated at 40 ml starting volume.

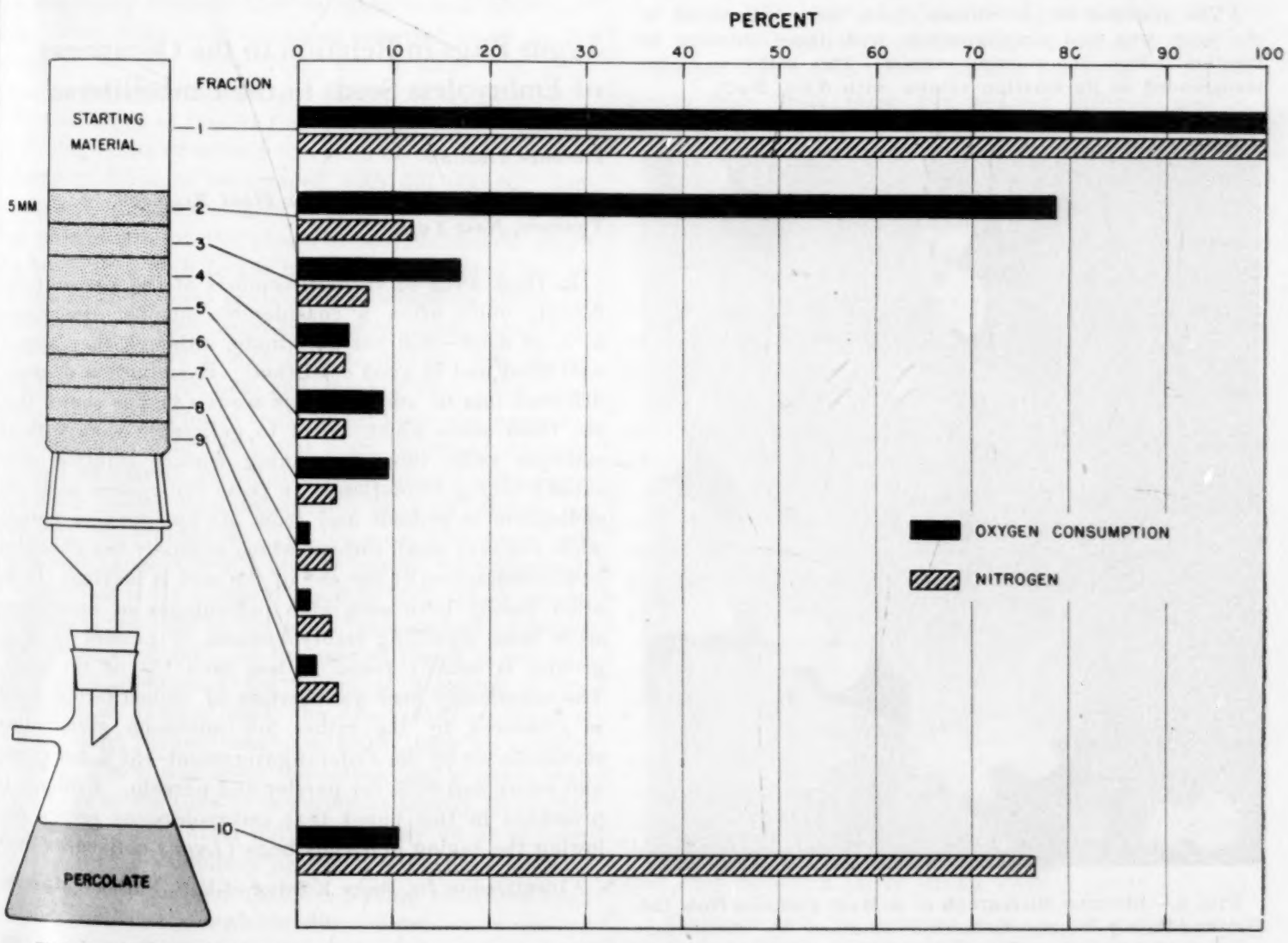

FIG. 3.—Distribution on the Celite column of melanized granules and other tumor components as indicated by the succinoxidase activity and the total nitrogen of the column eluates as compared with the percolate and the starting extract.

Preliminary studies have not shown any obvious staining or morphological differences in chromatographed granules as compared with smears or centrifuged preparations. There was, however, an apparent increase in uniformity of population. Fig. 4 shows an electron micrograph of Harding-Passey granules separated by flowing chromatography.[3]

The adaptation of chromatography to particulates ranging from virus to mitochondrial and bacterial size provides another method for separation and characterization of the particulate components of the cell. Since columnar chromatography presumably exploits the surface and molecular configurations of particles rather than their mass or specific gravity, the method may provide a new attack on the problem of separating morphologically similar units possessing different physical or chemical surfaces.

TABLE 2

RELATIVE DOPA OXIDASE ACTIVITIES PER UNIT OF NITROGEN IN S91 MELANOMA FRACTIONS OBTAINED BY PARTIAL CENTRIFUGAL PURIFICATION FOLLOWED BY CHROMATOGRAPHIC SEPARATION

Fraction	$QO_2(N)$ Value			
	Exp. 1	Exp. 2	Exp. 3	Mean
1. Starting extract*	23.5	13.1	14.2	16.9
2. Sedimented granules† ...	79.5	31.4	27.0	46.0
3. Column eluate‡	225.1	130.6	147.5	167.7
4. Sedimented granules from eluate§	372.4	185.4	78.1	212.0

* This extract prepared essentially as described in text footnote 2 except for being cleared twice at approximately 1,000 × gravity.

† This granule suspension consisted of all the material sedimented by subjecting the cleared starting extract to a force of approximately 4,000 × gravity for 10 min. The resulting pellet was resuspended to the original volume with 0.9% NaCl.

‡ The 10-fold increase in enzyme activity of this fraction compared with the starting extract has a $P < .001$ and is thus highly significant statistically. It is not known at present whether removal of an inhibitor is involved in this increase or not.

§ The granules in the column eluate were sedimented in the same way and simultaneously with those obtained in fraction 2 from the starting extract. This pellet was also resuspended to its starting volume with 0.9% NaCl.

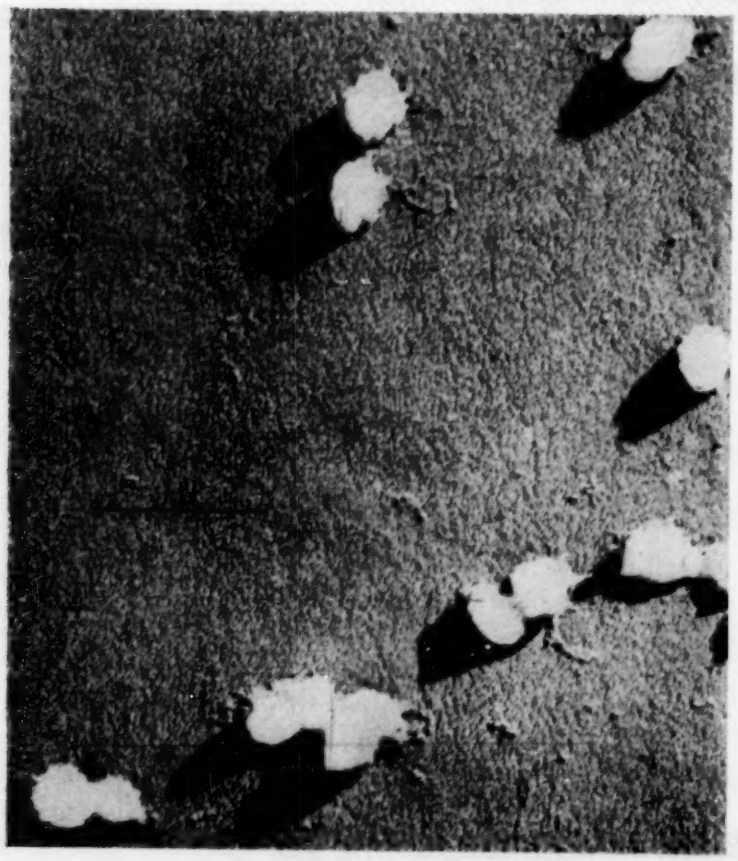

FIG. 4.—Electron micrograph of melanin granules from the Harding-Passey mouse melanoma obtained by chromatography. Gold shadowed at the approximate angle tangent 1/3. Magnification 8,000 ×. Enlarged to about 18,000 ×.

References

1. DUBUY, H., WOODS, M., BURK, D., and LACKEY, MARIE. *J. Nat. Cancer Inst.* Feb. 1949.
2. MASON, HOWARD S., KAHLER, HERBERT, MACCARDLE, ROSS C., DALTON, ALBERT J. *Proc. Soc. exp. Biol. and Med.*, 1947, **66**, 421–431.
3. RILEY, VERNON T. *Science*, 1948, **107**, 573–575.
4. STRAIN, HAROLD H. *Chromatographic adsorption analysis.* New York: Interscience, 1945.
5. WOODS, M., DUBUY, H., BURK, D., and HESSELBACH, MARIE. *J. Nat. Cancer Inst.* Feb. 1949.
6. ZECHMEISTER, L., and CHOLNOKY, L. *Principles and practice of chromatography.* New York: John Wiley, 1943.

Lygus Bugs in Relation to the Occurrence of Embryoless Seeds in the Umbelliferae

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In fresh seeds of various members of the Umbelliferae family, quite often a considerable number—sometimes 50% or more—will not germinate, although they appear well filled and in good condition. Examination of many different lots of umbelliferous seeds (*3*) has shown that the fresh seeds which failed to germinate were without embryos while those containing mature embryos gave satisfactory germination. In these embryoless seeds the endosperm is present and from all appearances normal while the very small embryo which normally lies imbedded in the endosperm at one end of the seed is lacking. In no other family have such high percentages of embryoless seeds been reported; embryolessness, if present in other groups, is usually found in less than 1% of the seeds. The notoriously poor germination of umbelliferous seeds is evidenced by the rather low minimum germination standards set by the Federal government—55% for carrot and celery and 60% for parsley and parsnip. Evidence is presented in this paper that embryolessness occurs following the caging of Lygus bugs (*Lygus oblineatus* Say[1]

[1] Identified by Dr. Reece I. Sailer of U. S. National Museum.

[3] Electron microscopy by Dr. Herbert Kahler and Mr. Bolivar J. Lloyd, National Cancer Institute.

and perhaps others) with the developing seeds of carrot and dill, and the results suggest that these insects are responsible for the natural occurrence of embryoless seeds in these species.

Lygus bugs are widely distributed and are known to feed on many of our native wild and cultivated plants. They reduce seed crop yields by causing bud blasting, as well as blossom and young fruit drop in alfalfa, beans, and cotton (*6, 8, 10*), seed spotting and pitting in the common and lima beans (*1, 4*), shriveled empty seeds in alfalfa (*2*), and reduced germination in beet, cotton, and guayule (*5, 7, 9*). As far as the writer is aware, a relationship between embryoless seeds in the Umbelliferae and Lygus bugs has not previously been observed.

In attempts to determine the cause of embryolessness, various possible factors, such as type of soil, locality, weather conditions, pollinating insects, and genetical influence, were studied but none of these seemed to have any bearing on the problem. Embryolessness was found to appear at random from year to year, with no correlation in regard to position on the plant or within the umbel (flower cluster). However, there was some indication that the seeds within a pair sometimes behaved similarly. Within a given sample embryolessness was present in seeds of all sizes. It was noted that embryoless seeds seemed to appear at a rather late stage of seed development, usually after the endosperm was more or less completely formed—that is, when it was white and firm. Very little embryolessness occurred early in the season at Yonkers, New York, but it was often quite prevalent in the midseason and early fall crops.

Various types of insects found visiting the flowers and developing fruits of various members of the Umbelliferae growing in Yonkers were caged with dill plants. Embryoless seeds almost invariably occurred, usually in very high percentages, on the plants or specific umbels which had been caged with Lygus bugs. Except for a few instances, no embryoless seeds were produced in either the control plants (caged insect-free) or in plants caged with other types of insects, such as ants, aphids, bees, Japanese beetles, lady beetles, and syrphid flies. The presence of a few embryoless seeds under these circumstances indicated either that the Lygus bugs, especially nymphs, were not effectively excluded or that other factors, perhaps other insects, may occasionally have an influence in producing embryolessness. In the open field where dill plants were exposed to all types of insects, the percentage of embryoless seeds ranged from 0 to 62%, while no embryolessness occurred in the seeds from umbels protected from insects by cages. In the case of plants caged with Lygus bugs throughout the period of flowering to the production of mature seed, the amount of embryoless seeds obtained ranged from 1 to 100%, with an average of 58%. There was some indication that contact with Lygus bugs at the time of flowering or shortly thereafter reduced seed yield, while contact for only 48 hr at later stages of seed development produced embryoless seeds.

These results establish that the feeding of Lygus bugs produces embryoless seeds in dill. Preliminary results with carrot were similar. Details of these experiments are appearing elsewhere.

References

1. Baker, K. F., Snyder, W. C., and Holland, A. H. *Phytopath.*, 1946, **36**, 493–503.
2. Carlson, J. W. *J. agric. Res.*, 1940, **61**, 791–815.
3. Flemion, F., and Uhlmann, G. *Contr. Boyce Thompson Inst.*, 1946, **14**, 283–293.
4. Hawley, I. M. *N. Y. (Cornell) agric. exp. Sta. Mem.*, **55**, 1922.
5. Hills, O. A. *J. agric. Res.*, 1943, **67**, 389–394.
6. McGregor, E. A. *U. S. D. A. tech. Bull.*, **4**, 1927.
7. Romney, V. E., York, G. T., and Cassidy, T. P. *J. econ. Ent.*, 1945, **38**, 45–50.
8. Shull, W. E. *Ida. agric. exp. Sta. res. Bull.*, **11**, 1933.
9. Smith, G. L. *Calif. agric. exp. Sta. Bull.*, **660**, 1942.
10. Sorenson, C. J. *Utah agric. exp. Sta. Bull.*, **284**, 1939.

A Metabolic Regulator in Mammalian Spermatozoa[1]

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The metabolic processes by which mammalian spermatozoa derive energy for motility have been a subject of investigation in this laboratory for some time. When the results of a series of studies (*8–15*) of the metabolism of bovine spermatozoa obtained from semen were compared with those of other investigators (*3, 4, 18, 19, 20*) who had studied epididymal spermatozoa, it became apparent that the metabolic pattern exhibited by bovine sperm cells from these two sources differed greatly. Since these workers (*3, 4, 18, 19, 20*) had used a wide variety of techniques and experimental conditions, a study was made (*7, 15*) of the metabolism of washed bovine epididymal spermatozoa in the calcium-free buffer-salts solution developed for ejaculated spermatozoa (*11*). Under these experimental conditions several metabolic differences between ejaculated and epididymal spermatozoa were observed. Those pertinent to the present discussion are:

(1) Most ejaculated spermatozoa have a vigorous endogenous respiration ($Q_{O_2} = 9$) (*10*). The addition of glucose results in a somewhat decreased rate of oxygen consumption (*8, 9, 12, 16*). In contrast, fresh epididymal spermatozoa have a comparatively low rate of endogenous respiration ($Q_{O_2} = 1$–4) while in the presence of glucose, respiration is appreciably greater ($Q_{O_2} = 2$–6) (*7*).

(2) Many specimens of ejaculated spermatozoa exhibit only a feeble Pasteur effect, *i.e.*, glycolysis in aerated media is almost as great as in the absence of oxygen (*8, 10, 14*). On the other hand, glycolysis by epididymal spermatozoa is 3–7 times faster under anaerobic conditions than it is in the presence of air (*7*). Certain specimens of ejaculated spermatozoa having a low endogenous respiration resemble epididymal sperm cells in that they exhibit a fairly strong Pasteur effect (*13, 14*)

[1] Published with the approval of the director of the Wisconsin Agricultural Experiment Station. This work was supported in part by a grant from the Rockefeller Foundation to C. A. Elvehjem and by the Badger Breeders Cooperative.

(3) Storage of excised epididymides alters their contained spermatozoa so that their metabolism more closely resembles that of ejaculated spermatozoa (7).

TABLE 1

AVERAGE RATES OF CATABOLIC REACTIONS IN BOVINE SPERMATOZOA*

	$-Z_{O_2}$		Z_L	
	Endogenous	+ Glucose	In air	In N_2
A. Epididymal	6	10	13	56
B. Ejaculated	20	16	20	25
C. Epididymal + regulator	20	22	20	35

* Z = mm³ gas exchange/100 million sperm cells/hr = 2.5 Q (*10*). Z_L = mm³ CO_2 equivalent to the lactic acid produced. The data represent averages of from 10 to more than 100 individual observations. Lactic acid was determined by the method of Barker and Summerson (*1*). Respiration measurements were made as described previously (*7, 11*).

Data summarizing these observations are included in Table 1, lines A and B, and in Table 2, line A. The data here are expressed in terms of Z values[2] instead of the more conventional Q values since cell counts are more conveniently made than dry weight determinations.

It is interesting to consider these metabolic data together with observations of motility. Epididymal spermatozoa with a Z_{O_2} of 6 move almost as vigorously as do ejaculated spermatozoa with a Z_{O_2} of 20. It appears, therefore, that the ejaculated spermatozoa are not as efficient in converting the energy of oxidative reactions to motion. The respiratory processes of the ejaculated spermatozoa are also less effective in depressing the rate of glycolysis.

A search for the cause of these differences in metabolic efficiency and for the phenomena described under (3) has led to the discovery of a metabolic regulator which is present in a bound (inactive ?) form in epididymal spermatozoa and which is apparently liberated in an active form soon after ejaculation. When small quantities of this regulator are added to epididymal spermatozoa an increased rate of respiration and aerobic glycolysis results immediately (Table 1, line C). The metabolism of epididymal spermatozoa in the presence of added regulator closely resembles that of ejaculated spermatozoa. Anaerobic glycolysis is usually depressed by the regulator, especially at higher concentrations. The response to a single level of the regulator is shown in Table 1, line C. Greater quantities depress respiration and glycolysis and abolish motility.

The biological activity of the regulator appears to result, at least in part, from its ability to uncouple exergonic oxidations from the phosphorylation reactions with which they are normally associated (*6*). The regulator resembles dinitrophenol in that it stimulates cellular respiration and aerobic glycolysis while preventing energy utilization (*2, 5, 14, 17*). We have devised an assay for the regulator based on its ability to stimulate the rate of aerobic fermentation by baker's yeast. Details will be presented elsewhere.

Using the yeast assay, it has been found that the regulator is present in a bound, inactive form in freshly ejaculated bull spermatozoa. During storage of semen at room temperature the substance is rapidly liberated from the spermatozoa into the seminal fluid in a water-soluble form which is still inactive for the yeast cell. The active substance is liberated from the water-soluble conjugate slowly during storage or more rapidly by mild alkaline hydrolysis. The substance liberated by hydrolysis is soluble in chloroform, ether, acetone, and petroleum ether. Alkaline hydrolysis is more effective in liberating the active form from the water-soluble conjugate than from the original bound form.

Fresh epididymal spermatozoa contain almost none of the free active regulator, but an appreciable quantity can be liberated by alkaline hydrolysis. When excised epididymides are stored in the refrigerator, the free form of the regulator is progressively released (Table 2). These results point to the likelihood that the increased rate of respiration of epididymal sperm following storage is brought about by the liberated regulator.

Furthermore, it seems probable that the free regulator liberated into semen after ejaculation is responsible for the higher rate of respiration of ejaculated spermatozoa as compared with epididymal spermatozoa.

We feel certain that the agent described plays an important role in the senescence of spermatozoa. If methods can be developed to prevent the liberation of the regulator or to counteract its effect once it is liberated, viable spermatozoa might be preserved for far

TABLE 2

EFFECT OF STORING EPIDIDYMIDES ON THE RESPIRATION OF THEIR CONTAINED SPERMATOZA, THE LIBERATION OF THE REGULATOR, AND THE RESPONSE TO ADDED REGULATOR*

Treatment	Time epididymides were stored at 5° C		
	3 hr	27 hr	51 hr
	$-ZO_2$		
A. Control	9	14.4	18.3
B. Plus regulator; 0.65 units/ml	20.3	20.3	22.4
	Units of regulator/10^8 sperm cells		
C. Boiled spermatozoa .	.04	...	0.7
D. Alkali-hydrolyzed spermatozoa	1.1	...	3.2

* One unit of regulator is the quantity required to give a half-maximum response in the standard yeast assay. Epididymal spermatozoa were washed with buffer-salts solution (*11*) before experimentation.

Respiration was measured in the presence of 0.01 M glucose.

Alkaline hydrolysis was carried out by suspending cells in 0.17 N NaOH and heating 10 min on boiling water bath.

[2] From the German "Zelle." The symbol was first used by Redenz (*18*).

longer periods of time than are now possible. The role of this regulator in sperm fertility is being studied.

References

1. BARKER, S. B., and SUMMERSON, WM. H. *J. biol. Chem.*, 1941, **138**, 535.
2. CROSS, R., COVO, G., TAGGART, J., and GREEN, D. E. *J. biol. Chem.*, in press.
3. HENLE, G., and ZITTLE, C. A. *Proc. Soc. exp. Biol. Med.*, 1941, **47**, 193.
4. HENLE, G., and ZITTLE, C. A. *Amer. J. Physiol.*, 1942, **136**, 70.
5. HOTCHKISS, R. D. *Adv. Enzymol.*, 1943, **4**, 153.
6. LARDY, H. A., and ELVEHJEM, C. A. *Ann. Rev. Biochem.*, 1945, **14**, 1.
7. LARDY, H. A., HANSEN, R. G., and PHILLIPS, P. H. *Arch. Biochem.*, 1945, **6**, 41.
8. LARDY, H. A., and PHILLIPS, P. H. *J. biol. Chem.*, 1941, **138**, 195.
9. *Ibid.*, *Amer. J. Physiol.*, 1941, **133**, 602.
10. *Ibid.*, 1941, **134**, 542.
11. *Ibid.*, 1943, **138**, 741.
12. LARDY, H. A., and PHILLIPS, P. H. *J. biol. Chem.*, 1943, **148**, 333.
13. *Ibid.*, 1943, **148**, 343.
14. *Ibid.*, 1943, **149**, 177.
15. LARDY, H. A., and PHILLIPS, P. H. *Nature, Lond.*, 1944, **153**, 168.
16. LARDY, H. A., and PHILLIPS, P. H. *Arch. Biochem.*, 1945, **6**, 53.
17. LOOMIS, W. F., and LIPMAN, F. *J. biol. Chem.*, 1948, **173**, 807.
18. REDENZ, E. *Biochem. Z.*, 1933, **257**, 234.
19. WINDSTÖSSER, K. *Klin. Wchschr.*, 1935, **14**, 193.
20. WOLF, C. G. *J. Physiol.*, 1921–2, **55**, 246.

Lack of Depolymerase Effect on Desoxyribonucleic Acid in Living Cells

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Biochemical Research Foundation, Newark, Delaware

Desoxyribonucleic acid depolymerase has been reported to remove ultraviolet light absorbing constituents and Feulgen stainable material, from nuclei in sections of tissue, and from nuclei of dead cells (*1*, *2*, *4*). There has been no reference in the literature, so far as the authors know, to the use of this enzyme on living cells.

In some experiments in this laboratory, it was found that the enzyme removed desoxyribonucleic acid from nuclei of chicken erythrocytes in smear preparations. After treatment with the enzyme, the nuclei failed to absorb ultraviolet light and did not stain with Feulgen's reagent. Addition of the enzyme to freshly obtained chicken blood, however, failed to affect the nuclei. This result suggested that perhaps living cells were unaffected by this enzyme when it was added to the extracellular fluid; results of further investigation showed that this is so with chicken erythrocytes and cells of Walker Carcinoma No. 256 of the rat.

Smears of chicken erythrocytes were fixed by immersion in 95% ethyl alcohol; they were then placed into fresh chicken blood to which had been added an equal volume of a solution of desoxyribonucleic acid depolymerase. The preparations were incubated at 37° C for periods of time up to 3.5 hr. In other experiments, suspensions of cells of Walker Carcinoma No. 256 of the rat in Ringer's solution were used in a similar manner. After incubation portions of the tumor cell-enzyme mixtures were transplanted into rats; if tumor growth followed it was assurance that the cells were living during the experiment.

The ultraviolet light (2654 A) absorbing material and the Feulgen stainable material in nuclei of the smears of both chicken erythrocytes and tumor cells were removed gradually and completely; however, there was no apparent effect on the nuclei of supposedly living chicken erythrocytes in the enzyme-blood mixture, or on the suspension of tumor cells. The tumor cells produced tumors after subcutaneous inoculation into rats; assuredly, they were living during exposure to the enzyme.

The enzyme attacked cells killed by heat, formaldehyde, alcohol, Carnoy's fixative, and ultraviolet light. Apparently the method of killing the cell makes little difference; it appears to be only necessary that the cell be dead for the enzyme to act.

Inability of the enzyme to act on the desoxyribonucleic acid of living cells might be explained by: a) absorption of the enzyme by cell constituents other than nucleic acid; b) antienzyme action; c) impermeability of cell membranes; d) inability of the enzyme to attack nucleic acid in the state that it exists in the living cell.

The possibilities that absorption and antienzyme activity prevented action of the enzymes on living cells were excluded by the fact that dead cells were acted upon by the same enzyme solution which failed to act on living cells. The assumption that membranes of the living cell are impermeable to depolymerase offers a plausible explanation for the lack of effect on living cells; however, it cannot be proved indisputably.

Whether or not other enzymes added to the exterior environment of living cells would fail to act on the respective substrates in cells is not known. Northrop (*3*), in 1926, reported that trypsin and pepsin were not taken up by cells of living organisms (earthworms, Euglena, yeast, meal worms, gold fish, and Fundulus), whereas, when the organisms died the enzymes were taken up rapidly from solution.

Desoxyribonucleic acid depolymerase did not act on nuclei of living chicken erythrocytes or of living cells of Walker Carcinoma No. 256 of the rat; the enzyme acted on these cells after they were killed. Lack of effect of the enzyme on living cells apparently was not because of adsorption of the enzyme or antienzyme activity, but may have been because of cell membrane impermeability or inability of the enzyme to attack nucleic acid in the state that it exists in the living cell.

References

1. BRACHET, J. *Symposia of the Society for Experimental Biology. I. Nucleic acid.* Cambridge: University Press, 1947.
2. CATCHESIDE, D. G., and HOLMES, B. *Ibid.*
3. NORTHROP, J. H. *J. gen. Physiol.*, 1926, **9**, 497.
4. STOWELL, R. E. *Stain Technol.*, 1946, **21**, 137.

NEWS and Notes

National Science Foundation. On March 31, April 1, April 4, and April 5 the Subcommittee on Public Health, Science, and Commerce of the House Committee on Interstate and Foreign Commerce held hearings on the several bills designed to create a National Science Foundation. Seven of the ten members of Mr. Priest's Subcommittee were on hand when the hearings opened, and both Mr. Crosser, chairman of the Committee on Interstate and Foreign Commerce, and Mr. Wolverton, who was chairman in the 80th Congress, sat through the entire session and participated actively in the proceedings.

Mr. Priest reviewed the history and status of the legislation before introducing Detlev Bronk, who developed the need for a Foundation to guide publicly supported basic research. Representatives of the Engineers Joint Council and the American Cancer Society also spoke in favor of the legislation, following a summary of the current British system of public and private support of research by Sir Robert Watson Watt.

Friday's hearings opened with the testimony of George E. Folk, advisor to the Committee on Patents and Research of the National Association of Manufacturers. Mr. Folk said that the NAM favors the creation of a National Science Foundation but he expressed a number of objections to specific features of the present bills. The seven speakers who followed Mr. Folk spoke much more briefly. Congressman James E. Van Zandt and Dean Harry P. Hammond, of the Pennsylvania State College Engineering school, testified in support of the bills. Chancellor R. G. Gustavson, speaking in behalf of the Association of Land-Grant Colleges and Universities and the National Association of State Universities, urged the principle of mandatory geographic distribution of research funds but said that he personally believed that provisions of the present bills, if carried out in good faith, would safeguard that principle. Boris A. Bakhmeteff, of the Engineers Joint Council, approved of both H.R. 12 and S. 247 but felt the Senate bill was more flexible and practical. Dael Wolfle, secretary of the Inter-Society Committee for a National Science Foundation, and Hugh Wolfe, of the Federation of American Scientists, suggested several specific changes recommended by the groups they represented. M. H. Trytten, director of the Office of Scientific Personnel of the NRC, presented statistics showing the need for the scholarships and fellowships which the Foundation would provide.

Congressman Celler, author of H.R. 359, was the opening witness on April 4. He was followed by Karl T. Compton, who endorsed the bills under consideration in the name of the National Military Establishment and its Research and Development Board. The patent provisions of the bills were attacked by Harold J. Kinney, a Minnesota patent attorney, and endorsed by Lawrence C. Kingsland, Commissioner of the U. S. Patent Office. Sidney Kirkpatrick, representing the Associated Business Papers, expressed fear that the Foundation's authority to disseminate research findings might result in government competition with scientific and trade publications.

Ex-Congressman Lanham testified on April 5. The hearings were then adjourned until April 26, when two hours' time will be allowed to testimony by representatives of the American Patent Council.

DAEL WOLFLE

Theodore von Karman, advisor on aerodynamics to the California Institute of Technology and the U. S. Air Force, is leaving this month for scientific conferences in Europe. Dr. von Karman recently resigned as director of Caltech's Guggenheim Laboratory of Aeronautics and chairman of the Jet Propulsion Laboratory Board, to devote more time to the Air Force and his own research and consulting work, but is continuing as advisor of the laboratories.

Charles T. Brues, professor emeritus of entomology, Harvard University, will spend the next nine months doing biological research at Silliman University, in the southern Philippines, under the auspices of the International Educational Foundation. Mrs. Brues, who is accompanying him, will make motion pictures of the plant and animal life of the region, under the sponsorship of the Fulbright Programs Branch of the U. S. Department of State.

Visitors to U. S.

Recent visitors from Britain include: **Sir Henry Tizard,** chairman of the Defense Research Policy Committee, Ministry of Defense, who came for the Massachusetts Institute of Technology mid-century celebrations; **S. Zuckerman,** University of Birmingham, and **R. L. Smith-Rose,** director of Radio Research, Department of Scientific and Industrial Research, now visiting radio research establishments in the U. S. and Canada. These men may be reached through the British Commonwealth Scientific Office, 1785 Massachusetts Avenue, N.W., Washington, D. C.

Edy Velander, managing director of the Swedish Royal Academy of Engineering Sciences, will arrive in this country, about the middle of April. He plans to attend the United Nations Scientific Conference on the Conservation and Utilization of Resources, in June, as a delegate from Sweden, and will also speak at a dinner meeting of the New York Section of the Institute of Food Technology on April 20.

Grants and Awards

Eileen R. Cunningham, librarian of Vanderbilt University School of Medicine, will be the first recipient of the **Marcia C. Noyes Award** of the Medical Library Association, to be presented at the Association's annual meeting, April 11, in Galveston, Texas.

The 1948 Lamme Medal of the American Institute of Electrical Engineers has been awarded to V.

K. Zworykin, vice president and technical consultant RCA Laboratories Division, Radio Corporation of America, Princeton, New Jersey, for his contribution to the concept and design of electronic apparatus basic to modern television. The medal will be presented to Dr. Zworykin at the Summer General Meeting of the Institute to be held in Swampscott, Massachusetts, June 20–24.

Colleges and Universities

The Premedical Society of the University of New Hampshire, Durham, was recently installed as the New Hampshire Alpha chapter of **Alpha Epsilon Delta.** Harold A. Iddles and Albert F. Daggett, department of chemistry, were initiated as honorary members, along with 32 premedical students. George Moore, department of zoology, will serve as faculty advisor.

Sigma Xi will install its 102nd chapter at Temple University, Philadelphia, on April 28. Installing officers will be Carl D. Anderson, national president of the Society, Nobel Laureate, and professor of physics at California Institute of Technology, and George A. Baitsell, executive secretary of the Society, and professor of biology at Yale University. The honorary degree LL.D. will be awarded to William H. Taliaferro, University of Chicago, and to Dr. Anderson, who will also deliver the installation address, "New Particles of Matter."

Western Reserve University's Department of Physiology is offering a new 12-month training course in the disciplines of cardiovascular research, supported by the American Heart Association and the National Heart Institute, U. S. Public Health Service. If the enrollment warrants, the course will begin July 1; otherwise it will begin September 1. Further information may be obtained from C. J. Wiggers, Western University Medical School, Cleveland 6, Ohio.

The **Four College Research Conference on Growth and Differentiation,** whose membership is drawn from the faculties of Amherst, Mt. Holyoke, Smith, and the University of Massachusetts, recently held its first meeting at Amherst. The organization, limited to active research workers whose projects are being supported by outside foundations such as the American Cancer Society, the Atomic Energy Commission, and the National Institutes of Health, offers an opportunity for intimate discussion of current research findings on growth and differentiation.

The Zoology Department of the **University of Massachusetts** is conducting an integrated interscience seminar on the Organization and Structure of Protoplasm. Discussions are presented by graduate students, members of the zoology, chemistry, and bacteriology departments, and by speakers from other universities, including E. W. Dempsey, of Harvard, Jytte Muus, of Mt. Holyoke, E. J. Boell, of Yale, and F. O. Schmitt, of the Massachusetts Institute of Technology.

Meetings and Elections

The Academy of World Economics announces that its 27th annual forum sessions will be held the evenings of April 12 and 13 at the Brookings Institution, Washington, D. C. The current sessions on "American Foreign Economic Policy" will be held in conjunction with the National Social Science Honor Society, Pi Gamma Mu, and with the Washington chapter of the American Political Science Association. The proceedings of the sessions will be published in the July issue of the quarterly journal *Social Science.*

The Foundation of Applied Research will hold a national conference on ova transplantation on April 14 in San Antonio, Texas. Phases in egg transfer and superovulation techniques will be discussed by biologists, embryologists, and geneticists, and a report on the Foundation's seven years of experimentation in ova transplantation, designed to enable scrub cattle to give birth to registered, high quality animals, will be made.

The Southeastern Section of the Botanical Society of America will hold its spring meeting April 14–16 in conjunction with the Association of Southeastern Biologists, the Southern Appalachian Botanical Club, and the Kentucky-Tennessee Branch of the Society of American Bacteriologists at the University of Tennessee, Knoxville. A Central States Section of the Botanical Society of America has recently been organized and has elected the following officers: Paul Weatherwax, Indiana University, president; Edgar Anderson, Missouri Botanical Garden, vice president; and Oswald Tippo, University of Illinois, secretary-treasurer. This new section will hold its summer meeting jointly with the Northwestern Section in late August at the University of Michigan and the Cranbrook Institute of Science.

The Association for Computing Machinery will hold a three-day meeting, April 18–20 at the Oak Ridge Institute of Nuclear Studies, Oak Ridge, Tennessee. This will be the third national meeting of the association. A "604" multiplier, recently developed by the International Business Machines Corporation, will be demonstrated.

Centre National de la Recherche Scientifique announces that a **Symposium on Thin Films** will be held in Marseille, France, April 18–23. American scientists invited are: John Strong, Department of Physics, Johns Hopkins University; A. F. Turner, Scientific Bureau, Bausch and Lomb Optical Company, Rochester, New York; Bruce B. Billings, Director of Research, Baird Associates, Inc., Cambridge, Massachusetts; and Noel W. Scott, Radiation Branch, Engineer Research and Development Laboratories, Fort Belvoir, Virginia.

The National Academy of Sciences will hold its annual meeting April 25, 26, and 27, at 2101 Constitution Avenue, Washington, D. C. A public lecture will be given April 25, at 8:00 P.M., by Sir Harold Spencer Jones, Astronomer Royal, Royal Greenwich Observatory, England. His topic will be "The Measurement of the Sun's Distance."

The Kansas Academy of Science will hold its 81st annual meeting at Kansas City College, Manhattan, Kansas, April 28–30. Cooperating societies are the Kansas Entomo-

logical Society, the Kansas Psychological Association, and the Kansas chapters of the American Association of University Professors.

The Society for Applied Spectroscopy will hold a symposium on "Theory and Application of Spectroscopy" May 21, at Brooklyn Polytechnic Institute, Brooklyn, New York.

The Fourth Annual AAAS-George Westinghouse Science Writing competition for an award of $1,000 to the writer of the outstanding newspaper story on science during the year 1949 has been announced. Another $1,000 will go to the writer of the outstanding magazine story of the year. Both awards, made possible by a grant from the Westinghouse Educational Foundation, are administered by the American Association for the Advancement of Science.

The rules governing the newspaper competition require each entrant to submit three separate articles published during the contest year (in newspapers published in the continental United States and dated between August 1, 1948, and September 30, 1949), and to designate one of the three as the entry upon which he wishes to be judged. All three may have been published by the same newspaper or carried by the same press association.

The magazine entries must have been printed in an American nontechnical magazine of general circulation and dated between August 1948 and September 1949, inclusive. Publications printing or distributing the winning newspaper and magazine articles will receive scrolls at the December meeting of the AAAS, when the winners of the 1949 awards will be announced. Although articles appearing in AAAS journals are automatically ineligible, readers of *Science* are invited to nominate suitable entries. All entries must be posted before midnight, October 8.

Entry blanks with detailed rules for the 1949 AAAS-George Westinghouse Science Writing Awards may be secured from the Managing Committee, Howard A. Meyerhoff, chairman, 1515 Massachusetts Ave., N.W., Washington, D. C.

Winners of the 1948 awards of $1,000 were Frank Carey, science writer in the Washington Bureau of the Associated Press, for his series of four articles on chloromycetin, and Florence Moog, of Washington University, St. Louis, for her article "The Biology of Old Age," published by the *Scientific American*.

Herbarium specimens of about 1,000 species have been collected on the Burma-India border during the past year by F. Kingdon-Ward on an expedition initiated by the New York Botanical Garden. The purpose of the expedition, begun early in 1948, is to obtain plant material, especially ornamental species, that will be suitable for culture in the U. S. To date, seeds of 260 plants have been received, none known to be cultivated in this country. The seeds have been distributed among the joint sponsors of the expedition—the New York Botanical Garden, the Huntington Botanical Garden of San Marino, California, Edward B. Stern of New Orleans, and Suydam Cutting of New York—and additional lots have been presented to growers in regions of the U. S. where they are expected to thrive.

The National Bureau of Standards' radio station WWVH, recently established on the island of Maui, Territory of Hawaii, is now broadcasting on an experimental basis continuous time and frequency standards on 5, 10, and 15 megacycles. The new station offers the Pacific area four useful technical services—standard radio frequencies, time announcements, standard time intervals, and standard musical pitch. WWVH's program of broadcasts is essentially the same as that of the Bureau's Beltsville, Maryland station WWV and it is expected that the new station may be received at many locations not served by WWV in the Pacific area. The ultimate aim of the International Telecommunications Union is to provide continuous world-wide coverage by means of suitably located stations all operating on the same frequencies without interfering with the widely used services from WWV.

University of Wisconsin scientists recently completed experiments which indicate that agene, the bleaching agent used in flour, is not a cause of human epilepsy, as has been thought. Collaborators on the experiment were C. A. Elvehjem, department of biochemistry, College of Agriculture; G. W. Newell and S. N. Gershoff, industrial fellows in biochemistry, T. C. Erickson, neurosurgery, and W. E. Gilson, medical electronics, School of Medicine. According to a report in the February *Journal of laboratory and clinical Medicine*, a control group of 19 persons, five of them epileptics, showed no ill effects after being fed a diet containing high concentrations of agene. The tests covered periods up to 210 days.

The National Society of Inventors, Inc., has established a Washington, D. C. chapter headquarters. Those interested in technological and engineering research and development may obtain further information from Lewis H. Renshaw, chairman, or John H. Haas, secretary-treasurer, 930 F Street, N. W., Washington, D. C.

The new national reactor testing station will be established on the Snake River plains of Idaho, the U. S. Atomic Energy Commission announces. Negotiations are under way with the Navy for the transfer to the Commission of the Naval Proving Grounds at Arco, which are included on the proposed site. The total area of the grounds will be about 400,000 acres, comparable in size to that of the Hanford plutonium production center on the Columbia River in Washington. All but about 20,000 acres are government owned land.

Make Plans for—

Southern Society for Philosophy and Psychology, April 14–16, Biloxi, Mississippi.

American Association of Pathologists and Bacteriologists, annual meeting, April 15–16, Boston, Massachusetts.

American Geophysical Union, 30th annual meeting, April 20–22, Washington, D. C.